The Journal

of the

Louisiana State Medical Society

$4.00 Per Annum, 35c Per Copy
Vol. 105, No. 7

JULY, 1953

Published Monthly
1430 Tulane Avenue, New Orleans 12, La.

THE ACUTE INFECTIOUS DIARRHEAS*

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It is particularly gratifying and a signal honor for me to be privileged to again speak before the Louisiana State Medical Society after a lapse of fifteen years. Although a similar subject is being presented, the passage of time has permitted a sober re-evaluation in the light of new developments. This is always a valuable criterion of the ever-changing and sometimes evanescent theories often prompted by enthusiasms of the moment. Let us then re-examine the general mechanism of acute intestinal infections and consider, in turn, bacillary dysentery, Salmonella disease, focal non-specific enterocolitis, viral dysentery, epidemic diarrhea of the newborn, and staphylococcal food poisoning.

The acute infectious diarrheas, theoretically, should include those due to an infecting organism, whether it be primarily enteric or extra-enteric. It is extremely doubtful that any bacterium or virus has any direct deleterious action on the intestinal mucosa merely by virtue of contact. Besredka's theory of local tissue immunity seems to make sense when applied to the intestinal mucosa which is constantly laved by pathogens or potential pathogens. It seems more likely that the noxious products of bacterial metabolism, such as toxins or viral agents, are absorbed through the intact intestinal mucosa and eventually reach all parts of the body. These are then excreted into the lumen of the bowel, perhaps in more virulent form, through the intramural intestinal arterial arborizations which end as a filamentous network to surround, embrace, and penetrate the solitary acuminate lymph nodules. These dot the entire gastrointestinal tract and serve as filtering or detoxifying mechanisms. We would naturally expect them to bear the brunt of injury and this is exactly what we find in Shigella and Salmonella disease. There is no convincing evidence that these lymphoid structures are injured by direct action of bacteria in the bowel lumen. In focal non-specific enterocolitis the focus is extra-enteric, usually in the upper respiratory tract, and for this reason fecal cultures are valueless.

BACILLARY DYSENTERY

Any consideration of this disease would be incomplete without the mention of Duval and Silverman, pioneers in the bacteriological and clinical studies on Duval (Sonne) infections. The present sharply rising trend in the incidence of acute bacillary dysentery can no longer be attributed to better diagnosis or reporting. These factors have been stabilized since 1934 when the disease was finally made reportable in all of our states. The graph (Figure 1) indicates that a peak of 38,313 cases was reached in 1944, followed by a precipitate drop to about 17,000 in 1947, only to be succeeded by a rapidly rising incidence which reached 32,425 in 1951, the last year of available public health statistics. From data at hand this cannot be attributed to returning Korean war veterans. It is unusual for the convalescent carrier state in

*Presented at the Seventy-third Annual Meeting of the Louisiana State Medical Society, New Orleans, May 9, 1953.

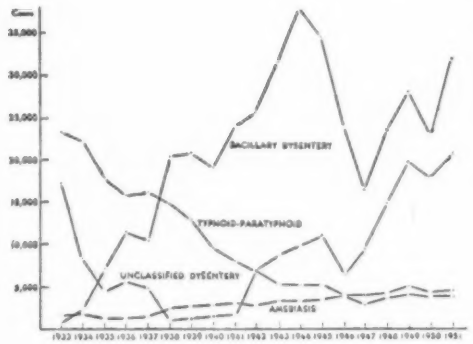

Figure 1

bacillary dysentery to exceed one month and, very rarely, one year. It is generally conceded that the reported incidence is but a fraction of the actual incidence. During the epidemic of Flexner dysentery in 1934[1] the proportion was about 1:20. We learned this during the Jersey City epidemic of 1934 by sigmoidoscoping all contacts, whether they had symptoms or not. To our great surprise, many had no complaints and yet exhibited the characteristic intestinal lesions, positive culture, a rising agglutination titer and positive phage. These individuals were potentially more dangerous in spreading the infection than the sick patients who were confined to bed. Failure of clinical recognition and procrastination in culturing patients with diarrhea appear to be the real reasons for the rising incidence of bacillary dysentery.

The difficulties in clinical diagnosis rest chiefly with the atypical cases, 7 of which it was our privilege to describe—the constipated, afebrile, asymptomatic, appendicular with acute distal ileitis, pneumonic, meningitic and agranulocytoid. It was the last 4 which led us to regard bacillary dysentery as a systemic disease with focal intestinal manifestations. The extra-enteric symptoms and signs dominated the clinical picture at the onset and most infective period of the disease. All exhibited the characteristic 3-stage progression of intestinal pathology, namely, punctate follicular hyperplasia, punctate follicular necrosis and discrete and confluent ulceration on the first, second, and third days of the disease.[2] This was accompanied by positive cultures, a rising agglutination titer, diagnostic phage and a typical purulent cytology of the mucosal exudate. These observations clearly indicate that in acute bacillary dysentery all contacts must be examined. We would then be in a better position to control the disease and understand the relationship to chronic ulcerative colitis and ileitis. In a study of 1,072 cases of the latter diseases (chronic ulcerative colitis 994, ileitis 31, combined form 47) we obtained 75 (7 per cent) positive cultures for *B. dysenteriae*, as compared with 0.08 per cent in 6,000 controls. Impressive epidemiologic data was secured in 236 cases.

Bacteriologic identification of the dysentery (Shigella) strains has outstripped clinical recognition and control. Due largely to the work of Boyd, supplementing the previous studies of Andrews and Inman, we now recognize 19 serologic types of the Flexner bacillus, in addition to the Shiga-Kruse, Schmitz, Sonne-Duval and alkalescens organisms. The Large-Sachs group is relatively rare. All are pathogenic for man. One observation may be of interest. The Shiga-Kruse organism, formerly very prevalent and virulent, particularly in the Far East, is now relatively infrequent. The Flexner and Sonne-Duval strains now appear to be dominant throughout the world, an example of biologic disease adaptation by both the infecting agent and host. We may confidently expect the return of Shiga-Kruse infections in the near future. The same phenomenon is evident in therapy where sulfonamid-resistant and, more recently, antibiotic-resistant dysentery strains are being encountered. At the present writing terramycin, chloramphenicol, and aureomycin appear to be effective against most dysentery strains, and Silverman[3] has found bacitracin therapy curative in chronic bacillary dysentery.

The relationship of bacillary dysentery to chronic ulcerative colitis and ileitis is still a controversial subject. Most serious students of the subject acknowledge that *some* but not all are due to bacillary dysentery. The differences of opinion are due largely to inadequate study of the acute cases, fail-

ure to recognize many of them clinically and paucity of follow-up data. Our follow-up studies[4] of the Jersey City epidemic of 1934 revealed an incidence of 10.7 per cent among 122 of an initial group of 210 hospitalized patients. These are based upon accurate observation of our best experimental subject, the human being. We followed the disease in the same patients from the initial phase of acute bacillary dysentery to the fully developed stage of chronic ulcerative colitis and ileitis at the end of nine to twelve months. This work has been confirmed elsewhere.[5]

Two other subjects of recent interest in connection with chronic ulcerative colitis are the relationship to carcinoma of the colon and to pregnancy. The first is particularly controversial, Bargen[6] and others holding that a relatively high incidence of carcinoma occurs in ulcerative colitis.

There is no doubt that carcinoma occurs in ulcerative colitis but our studies and those of Snapper and Otani fail to indicate any relationship. There is no evidence that the pseudo-polyposis of ulcerative colitis develops into carcinoma in situ or otherwise, such as one sees in adenomatous polyps. In 1,072 of our cases, carcinoma occurred in 7 (0.65 per cent) as compared with 0.8 per cen in 12,025 general admissions without ulcerative colitis at the Bronx Hospital during 1946 and 1947.

Pregnancy appears to have a rather salutory effect on a pre-existing chronic ulcerative colitis. Our own experience covers 117 pregnancies occurring in 72 patients. During 50 of these pregnancies the patients felt well symptomatically and this state was reflected by improved or absent sigmoidoscopic findings. In 39 pregnancies the patients were not well but without any significant influence on the pregnancy. In 5 patients the disease started during pregnancy and these are included in the group of 39. Their disease was no worse than in the other 67 patients in whom it antedated the pregnancy. In 8 pregnancies the colitis was definitely worse after delivery but quiescent during pregnancy. In 11 instances the data was incomplete.

SALMONELLA DISEASE

Next to acute bacillary dysentery, Salmonella disease appears to be the most prevalent infectious diarrhea throughout the world.

There are several points of similarity between the Shigella (dysentery) and Salmonella infections. Both are transmitted "from hand to mouth" or more properly "from intestine to mouth," the chief vehicles being the three F's—food, fingers and flies. Adaptations to the human host leading to increasing prevalence and pathogenicity have occurred in Sonne-Duval infections and *B. alkalescens* just as they have developed in the case of the present 150 or more Salmonella strains. The heterogenicity of the Shigella strains are paralleled by the even more complex Salmonella genus. The intestinal lesions primarily involve the lymphoid structures in both diseases. Epidemiologic measures involve the same factors. These observations indicate that measures directed at the control of acute bacillary dysentery should at the same time effectively control Salmonella infections. These two diseases constitute the vast majority of infectious diarrheas due to known enteric pathogens and their incidence is closely paralleled by the prevalence of unclassified dysenteries. The latter drop sharply when carefully studied since most of them appear to be bacillary dysentery. It strikes us, therefore, that *all* should be handled with the same meticulous care as we do typhoid. Measures directed at typhoid alone have failed to control the Shigella and other Salmonella infections.

We now recognize more than 150 Salmonella strains pathogenic for man. As in acute bacillary dysentery, the reported incidence is probably far below the actual incidence. Many cases are unrecognized because of their relative mildness. On the basis of antigenic analysis (0 or somatic antigens) the Salmonellae have been divided into five main groups and many subgroups (on the basis of H or flagellar antigens). Representatives of the main groups are shown in Table 1.

TABLE 1
CLASSIFICATION OF SALMONELLA STRAINS

GROUP	SALMONELLA
A	Paratyphi A
B	Paratyphi B (Schottmülleri)
	Typhimurium
	Derby
C	Choleraesuis
	Oranienberg
	Montevideo
	Newport
D	E. typhosa
	Enteritidis
E	Panama
	Ananatum
	Seftenberg
	Give

The most frequent source of Salmonella infection is domestic animals, particularly fowl and swine. The organisms are found in both diseased and healthy domestic animals, the latter including carriers such as rats and mice. They have also been demonstrated in the mesenteric lymph nodes of normal hogs, in normal hens, and in dried eggs. In Europe, duck's eggs are frequently implicated and, in Norway, cheese. They occur in meat products, particularly hog's liver. Sewage is a prolific source of Salmonella infection. Many types of birds are carriers and many harbor the organism in the ovaries or testicles.

In man, the most frequent source of Salmonella infection appears to be food animals. Infected meat—food contaminated by sewage, infected foodhandlers, or by the excreta of rodents—is frequently the source of outbreaks. The most serious outbreaks have been due to ingestion of meat of animals that have died with the septicemic type of disease or to safe food which has been contaminated and stored under conditions which permit the rapid growth of an otherwise numerically low bacterial population. *S. paratyphi A* and *S. choleraesuis* cause sporadic cases while *S. typhimurium*, *S. paratyphi B* and others are usually related to outbreaks. *S. typhimurium* causes more individual cases than outbreaks through food, milk and water, while *S. paratyphi B* is apt to be responsible for contact infections.

Human carriers play an important role in the dissemination of Salmonella infections. The subject of typhoid carriers requires no reiteration. In a recent outbreak at a summer camp in Far Rockaway, New York, 40 cases of typhoid were traced to a cook. Nine contact cases were discovered during the course of a careful epidemiologic investigation[7] without clinical symptoms or signs. Chronic human carriers of Salmonella strains of animal origin are rare. *S. typhimurium* and *S. choleraesuis* are the most prevalent representatives of the animal group and *S. paratyphi B* of the human group. *S. paratyphi B* may be present in the gall bladder of a carrier for a long period of time and may also be excreted through the urinary tract. Carrier states for other than *S. paratyphi B* and *S. typhi* infections are generally shorter and terminate spontaneously.

All age groups are susceptible to Salmonella infection, but the very young are particularly so, with an attendant high mortality. Approximately 30 per cent of all sporadic infections occur during the first decade, chiefly with *S. typhimurium*, *S. paratyphi B*, *S. oranienberg* and *S. newport*, in order of diminishing frequency.

The seasonal incidence of Salmonella infections corresponds to that of bacillary dysentery. It is highest during the warm season and lowest during the cold, paralleling the prevalence of the fly population.

There is a paucity of clinical data regarding most Salmonella infections except typhoid and paratyphoid. The reason lies in the relative mildness of the illness in many instances, the failure to recognize the disease, and almost complete absence of sigmoidoscopic and pathologic data.

Salmonella infection should be regarded as a systemic disease with focal intestinal manifestations. This concept, similar to that proposed for Shigella infections, explains many of the bizarre clinical pictures encountered, such as the typhoid-like, appendicular, pneumonic and meningitic types. The last two are merely extra-enteric lesions which dominate the clinical manifestations, often to the exclusion of diarrhea. Variations in pathogenicity and

virulence largely determine the severity of the disease and the ultimate outcome. Age is also a factor, the two extreme age groups being most susceptible and exhibiting the highest mortality. Similarly, malnutrition and illness are contributory factors to morbidity and mortality. The incubation period for most Salmonella infections is eight to twenty-four hours. The minimal period is somewhat less.

A convenient clinical classification of the typical Salmonella infections is that comprising the (1) intestinal, (2) febrile, and (3) septicemic types. They overlap somewhat, many patients exhibiting features of all three.

The intestinal type of Salmonella infection is usually mild in adults. It is ushered in by a feeling of malaise and nausea or vomiting. This is followed by a mucoid or watery diarrhea which is generally accompanied by abdominal cramps of moderate severity. Intestinal bleeding is infrequent. Sigmoidoscopy reveals a diffuse reddish blush to the mucosa which is sometimes studded with whitish hyperplastic lymph nodules. Superficial mucosal erosions and some punctate follicular necrosis may be present. The three-stage progression of intestinal pathology and purulent mucosal exudate, typical of acute bacillary dysentery, are usually not seen, the lesions being most marked in the lymph nodules. Spasm and tenderness of the terminal ileum and sigmoid may be noted upon deep abdominal palpation. Such manifestations in the right lower quadrant may simulate acute appendicitis. Fever is moderate and of short duration, and recovery is generally complete in one week in the adult. Infants are more seriously affected, with an attendant higher mortality. *S. typhimurium* and *S. enteritidis* appear to be most frequently implicated in the intestinal type of Salmonella infection.

The febrile type resembles typhoid fever, particularly in *S. paratyphi A, B* and *C* and *S. sendai* infections. Fever is usually the most prominent clinical feature but by no means the only one. Suggestive rose spots, a leukopenia, slow pulse and splenomegaly usually impel the clinician to resort to blood culture, Widal tests and stool cultures in order to rule out typhoid. Blood cultures are more frequently positive early and stool cultures or Widal tests late in the course of both the febrile type of Salmonella infection and typhoid. Except in *S. paratyphi B* infection, the mortality incidence is low. The clinical course varies from three to five weeks. Misleading pulmonary or appendiceal symptoms and signs may confuse the clinical picture. *S. paratyphi A* and *B* are most frequently encountered in the febrile type of Salmonella infection.

The septicemic type presents a clinical picture like that seen in bacteriemia by pyogenic cocci. The intestinal manifestations are minimal or absent. The febrile reaction is of the "spiking" variety and focalization may occur in the meninges or bone. Blood cultures are positive and the mortality incidence is high. *S. choleraesuis* is the most frequent cause of this type of the disease.

Among the atypical forms of Salmonella infection are the appendicular, pneumonic, meningitic, and asymptomatic. They are less distinctive than similar types seen in acute bacillary dysentery. Their significance lies chiefly in the clinical and epidemiologic implications. The pneumonic and meningitic types differ from those of bacillary dysentery in that the specific organism can be recovered from the sputum and meninges, respectively, when Salmonella is the infecting agent.

Complications of Salmonella infection are cholecystitis, empyema of the gall bladder, salpingitis, pyelonephritis, bacterial endocarditis, and osteomyelitis. Complications are rare in adults, more common in infants and children. Middle aged females are apt to retain *S. paratyphi B* in the gall bladder for long periods of time and thus may become chronic carriers.

The distribution and character of the pathological lesions in the intestines resemble those seen in typhoid. In one instance, at the Bronx Hospital, that of an adult who succumbed to an infection with *S. panama*, the major pathology was seen in Peyer's

patches and the solitary acuminate lymph nodules of the ileum and colon. Varying degrees of hyperplasia and necrosis were noted, with scattered small superficial erosions of the mucosa. There was marked congestion of the mucosal and submucosal vessels with some accompanying round-cell, plasma-cell and polymorphonuclear-cell infiltration. A striking feature was the absence of the cellular barrier at the base of an ulcerated area as seen in acute bacillary dysentery. The mesenteric and mesocolic lymph nodes were enlarged and exhibited varying degrees of lymphoid hyperplasia, focal necrosis, interstitial edema and lymph stasis. Similar findings were present in the spleen. Changes in the other organs were noted, such as cloudy swelling of the renal epithelium, pulmonary congestion, fragmentation of the myocardial fibers and interstitial edema. The general pathologic changes suggested a severe toxic process, death occurring three days after the onset of the infection. Two daughters with the same infection survived. Our sigmoidoscopic studies in milder cases of Salmonella infection have generally revealed a diffuse hyperemia of the mucosa with lymphoid hyperplasia or punctate follicular necrosis. The picture resembles that seen in intestinal allergy except for involvement of the lymph nodules and absence of eosinophiles in the mucosal exudate.

Chloromycetin (chloramphenicol) and terramycin appear to be the most effective antibiotics in typhoid and other Salmonella infections. In one instance, at the Bronx Hospital, Mond[8] reports the prophylactic value of chloramphenicol in the case of a newborn infant born of a typhoid carrier. Zimmerman, Cooper and Graber,[9] in recent studies in Korea, found that *S. paratyphi, S. typhimurium* and *S. paratyphi B* (*schottmülleri*) were equally sensitive to both antibiotics mentioned above. Very few strains were sensitive to aureomycin. Because of wide variations in the susceptibility of the many Salmonella strains to antibiotic agents, it is advisable to test out specific isolated cultures routinely. The divided culture plate[10] is a convenient and economical method.

The greater portion of this paper has been devoted to the two major infectious diarrheas, viz., bacillary dysentery and Salmonella disease due to primary enteric pathogens. In concluding this presentation we shall briefly describe a group of infections which has attained clinical significance comparatively recently—acute focal nonspecific entercolitis, viral dysentery, staphylococcal food poisoning and epidemic diarrhea of the newborn.

FOCAL NONSPECIFIC ENTEROCOLITIS

Acute focal nonspecific enterocolitis may be defined as an acute inflammation of the ileum and colon due to a toxin, bacterium, or virus produced in some extra-enteric focus. Diarrhea is generally the most prominent feature. Abdominal pain may be present and is usually located in the right lower quadrant. Tenderness can often be elicited over the distal portion of the ileum and sigmoid. The bowel movements are usually of watery consistency, may contain mucus, rarely blood. There is always an initial associated infection elsewhere in the body. The intestinal symptoms and signs follow the onset of that infection, often last somewhat longer but usually subside with resolution or eradication of the primary extra-enteric disease. The chief clinical features are generally those of the primary infection but the latter may be overshadowed by those of the secondary focal enterocolitis. Recurring attacks of the primary disease are apt to be followed by a repetition of the intestinal manifestations in each instance, particularly in the case of respiratory infections or sore throat in children. Cessation of the recurring attacks of the primary disease is paralleled by the disappearance of further intestinal symptoms. The prognosis is that of the primary disease except that infants sometimes die with dehydration, acidosis, and hypovitaminosis as a result of the frequent watery bowel movements.

The intestinal lesions vary from hyperemia and edema of the mucosa with lymphoid hyperplasia to superficial mucosal erosions. Considerable mucoid exudate is

present, the cytology including lymphocytes, some polymorphonuclear cells, and eosinophiles. Mesenteric lymphadenitis may be noted. Sigmoidoscopic crypt aspiration culture is negative for the specific enteric pathogens of the Salmonella-Shigella group.

Aside from the frequent intestinal manifestations seen in association with upper respiratory infections in infants and children, similar observations have been made in adults. A striking example was the case of a young pharmacist whose frequent attacks of "colitis," over a period of years, were always associated with tonsillitis. Pus could be expressed from the crypts. Sigmoidoscopy revealed a hyperemic, boggy mucosa in the recurrent phase and appeared normal when the tonsillitis subsided. Tonsillectomy resulted in complete freedom from intestinal symptoms and signs during a follow-up period of nine years.

The treatment of focal nonspecific enterocolitis is that of the primary extraenteric disease. The absorbable sulfonamides or suitable antibiotics may be used, depending upon the nature and sensitivity of the infecting organism. In babies, phleboclysis, transfusion of whole blood, lyophile plasma and other supportive measures must be used early, for the margin of safety between life and death is exceedingly narrow.

VIRAL DYSENTERY

Viral dysentery was described by Reimann, Hodges and Price[11] as occurring in epidemic form and consisting of diarrhea, nausea and vomiting. It was regarded as due to a viral agent. Experiments on medical students pointed in this direction. Fresh, filtered broth garglings and suspensions of diarrheal stools from sick patients were administered to the experimental subjects. The nebulized filtrates were inhaled in a closed container. Within a few days many of the students developed malaise, headache, abdominal discomfort, nausea, vomiting and diarrhea. Some had a nasopharyngitis. No symptoms followed the ingestion of gelatin capsules filled with filtered material obtained by gargling or with filtered fecal suspensions. The investigators concluded that the noxious agent was a filtrable virus which was air-borne and entered the body through the respiratory tract. It was present in the oropharynx and intestinal tract. It appears quite probable that viral dysentery falls into the preceding group of focal nonspecific entercolitis in which the primary focus is in the upper respiratory tract. The infection reaches the intestinal wall through the indirect hematogenous excretory mechanism. Both the experimental and clinical data lend support to this view.

EPIDEMIC DIARRHEA OF THE NEWBORN

Epidemic diarrhea of the newborn occurs during the first two or three weeks of life, is most prevalent in the north temperate zone, and affects chiefly premature and artificially fed infants. It occurs in hospitals and affects groups of infants. The clinical picture is characterized by the sudden onset of diarrhea in a previously healthy infant. In some instances there may be prodromal symptoms such as vomiting, arrested weight gain, listlessness, and anorexia. Diarrhea, accompanied by slight fever, dehydration, frequent respiratory and otitic complications, and a high mortality (almost 50 per cent in some outbreaks) comprise the chief clinical manifestations. The cause is unknown. In one outbreak coagulase-positive *Staphylococcus aureus*[12] appeared to be of etiologic significance. Other investigators have implicated *B. coli, B. morgani, B. dysenteriae,* streptococcus, *B. mucosus* and pneumococcoccus. In the outbreak referred to above, there was no mortality among 19 babies affected. This surprising result appeared to be due to the use of sulfathiazole and concentrated lyophile plasma both prophylactically and for curative purposes. Sick infants were given 6 gr. of sulfathiazole thrice daily for two days, followed by 3 gr. thrice daily for two days. They also received 50 cc. of plasma of normal concentration, subcutaneously as an initial dose. Thereafter, 25 cc. of twice concentrated plasma (ie., adding half the amount of distilled water normally used) was injected intramuscularly daily for three days. Prophylactic sulfathiazole therapy for contacts was started when the

newborn was 48 hours old and consisted of 3 gr. thrice daily for three days. This was supplemented by 25 cc. of plasma of normal concentration subcutaneously daily for three days. No contact infections developed. It is quite possible that epidemic diarrhea of the newborn falls in the group termed "focal nonspecific entercolitis." In recent years the disease appears to have lost much of its initial severity and high mortality.

STAPHYLOCOCCAL FOOD POISONING

Staphylococcal food poisoning is generally due to contamination of custard or similar foods by a food handler with a staphylococcal skin infection. Subsequent environmental conditions favoring the production of toxin by the viable cocci produce an acute clinical syndrome characterized by fever, vomiting, diarrhea, cramps, and marked prostration. The clinical course is usually brief, being a matter of one to three days, and the mortality negligible in adults. Sigmoidoscopy in one instance revealed an evanescent moderate, diffuse hyperemia and edema of the mucosa. Resterilization of custards and similar foods as a routine procedure is advocated as a preventive measure.

The causative agent is an enterotoxin produced by coagulase-positive hemolysin and rich pigment producing strains of *Staphylococcus aureus*. The organism is particularly pathogenic for young kittens. These animals are inoculated by the peritoneal route, according to the method of Dolman, Wilson and Cockcroft.

SUMMARY

Bacillary dysentery continues in high incidence and we have indicated its relationship to chronic ulcerative colitis. This alone should justify stern control measures, such as those employed in typhoid. Shigellosis is accompanied by a parallel increase in Salmonella disease, often unrecognized and unreported. The clinical and pathological features of both have been presented. The more recently described infectious diarrheas are those due to primary extraenteric infective agents, viral dysentery, epidemic diarrhea of the newborn, and staphylococcal food poisoning.

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MANAGEMENT OF OTITIS MEDIA; ANTIBIOTIC THERAPY VERSUS SURGICAL PRINCIPLES*

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BATON ROUGE

Otitis media has never been an easy disease to treat, and the results of therapy have always left something to be desired. That explains why, when the sulfonamides were introduced and were followed in turn by the various antibiotics, otolaryngologists seized upon them so eagerly as the solution of this problem. All of us, I am afraid, were equally guilty. None of us is in any position to cast stones. It seems fair to say, however, that some of us have not yet emerged from the dream.

The facts of the matter are that these agents have not proved the panacea for which we sought in otitis media, and that they have, on the contrary, proved both delusory and dangerous. This is not, of course, because they have failed. The failure

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*Presented at the Seventy-third Annual Meeting of the Louisiana State Medical Society, at New Orleans, May 9, 1953.

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is human. The sulfonamides and antibiotics have been used indiscriminately and unwisely. They have been employed in a disease in which they could not be expected to be effective. It has been almost entirely forgotten that these agents, because of their biologic properties, are capable of relieving the symptoms of otitis media while at the same time the pathologic process which gives rise to the symptoms may continue only partly checked, or entirely unchecked, with results that may be disastrous.

It is ironic that otolaryngologists were warned of these dangers almost as soon as the new chemotherapeutic era began. In 1939, less than two years after sulfonilamide had first been used clinically in this country, Maybaum and his associates,[1] from Mt. Sinai Hospital in New York, warned of the dangerous masking potentialities of this drug and proved this point with a number of highly instructive case reports. Two years later, in 1941, when the swing to the new drugs was in full flood, Fowler[2] spoke out even more strongly. Chemotherapy, he said, had become the medical fashion, and patients were themselves demanding this new method, though a large proportion of the cures attributed to it were really spontaneous remissions. Any physician, he continued,

> "who in shot-gun fashion prescribes a drug in all cases without discrimination is reflecting ignorance, laziness or poor judgment as to the expectancies of serious trouble from otitis media. He may sensitize his patient, damage his liver or kidneys, or render him drug-fast while using chemotherapy for a minor ailment, which at a later date might then be unavailable for a serious infection."

It is extremely unfortunate that those early warnings were not heeded. If they had been, our present difficulties would not have come to pass. We are now in the ironic position of being called upon to treat not only patients with primary otitis media whom we are fortunate enough to see early, but also, (1) patients with the complications of neglected disease, and (2) patients with the therapeutic complications of mistreated disease. These latter complications do not occur in the natural course of otitis media. They occur because the primary disease is masked by a mistaken faith in chemotherapeutic and antibiotic agents.

Let me cite our own recent experience, and let me assure you that the literature is full of the records of many similar experiences. During the past January, which was a typical winter month, we saw in our office 55 patients, chiefly children, suffering from otitis media for which myringotomy was indicated. Thirty-four of the patients had had no previous treatment. They were all submitted to myringotomy and they all recovered promptly, with no further treatment other than standard measures, in an average of 5.17 days.

The remaining 21 patients had all been treated previously by chemotherapeutic or antibiotic agents, without myringotomy. They sought medical relief because their ears had failed to heal, or because of continuing or recurrent infection. Like the group of patients just mentioned, all were submitted to myringotomy. But their recovery took, on the average, 13.55 days. Furthermore, 9 of them required the use of antibiotics, which were not employed until after their effectiveness against the organisms present had been proved in the laboratory.

It seems unnecessary to labor the point that an experience such as this calls for an evaluation of present methods of treatment of otitis media, especially on the part of otolaryngologists and other physicians who have been trying to manage this disease without the use of myringotomy.

FALLACIES OF PRESENT THERAPEUTIC METHODS

The present situation in the therapy of otitis media may be described about as follows:

1. History-taking is likely to be superficial. Local examination is likely to be equally superficial. In a startlingly large number of cases no attempt is made to examine the tympanum or, if rupture has occurred, to clean out the canal. Instead, there is a rather general tendency to administer penicillin to all patients, and particularly to all children, with symptoms referable to the ear and associated with fever

and other evidences of a constitutional reaction. Sometimes only a single injection is given. Sometimes the original injection is repeated once or twice. Sometimes a sulfonamide or some other antibiotic is administered also.

2. The drugs administered usually relieve symptoms promptly. Pain disappears and the temperature falls. Often the improvement is so dramatic that the adult does not return for further observation and the child is not brought back to the office. Parents, incidentally, are now so conditioned to the present methods of treatment that they demand them if the physician does not offer them himself. Their faith in the antibiotics, particularly penicillin, is also so great that they confuse the disappearance of symptoms with the elimination of infection, a confusion, it is fair to say, in which they are frequently joined by many general practitioners and pediatricians and even by some otolaryngologists.

3. In a large number of cases treated in this manner, cure really does occur, and the antibiotics receive the full credit for it. This is because it is generally forgotten that otitis media is a self-limiting disease and that the great majority of infections which respond to this sort of superficial therapy would have disappeared with the passage of time and the use of standard measures, or with no therapy at all. Four-fifths of all patients with this disease will recover spontaneously if suppuration has not occurred.

4. In a number of cases of otitis media, however, after the initial period of improvement, signs and symptoms of infection again become evident. There is nothing surprising about this. With the sort of treatment employed—antibiotics in small dosages over a brief period of time—bacteriostasis is incomplete and bactericidal activity does not occur at all. The patients themselves have no antibacterial elements in their blood. Natural immunity is not acquired when these drugs are used, and the organisms regain their former harmful properties if they are discontinued too soon. In many such instances the acute infection is merely transformed into a chronic infection and the patient may be left with a chronically discharging ear.

5. Mistreated otitis media is apparently becoming an important cause of otitis externa. When I reviewed my records of this disease in 1949, I was not particularly impressed by this etiologic factor. In a review of 157 cases which I have recently completed, I found that in 28 cases chronic middle ear disease was the apparent cause of the infection of the external ear.

6. In the occasional case far more serious things happen. Clinical improvement occurs, but the pathologic process, completely masked by the antibiotic agents used, continues inexorably, to present as mastoiditis with almost complete bony breakdown, meningitis, epidural or perisinal abscess, lateral sinus thrombosis, or brain abscess. I see two to four such cases every year myself, and the number recorded in the literature has now mounted to a sizeable total.[3]

7. Possibly my own keen interest in deafness in children is responsible for my feeling that one of the most disturbing consequences of mistreatment of middle ear disease is its effect on hearing. I have long believed that most of the so-called adhesive deafness of adult life is the result of inadequate treatment of otitis media in childhood. I am now modifying that long-held opinion with the prophecy that if we do not promptly change our therapeutic policies, we shall find that much of adult deafness is the result of the misuse of antibiotic and chemotherapeutic agents in otitis media in childhood.

Repeated attacks of otitis media are probably the commonest cause of conduction deafness in children. When the primary infection is only incompletely resolved, as it frequently is when it is inadequately treated with even the most potent of the new agents, adhesions form in the ossicular chain or between the tympanic membrane and the promontory, and the regional mucosa becomes thickened and fibrotic. The physician who takes the trouble—not all do—to examine the tympanic membrane will

find it dull, thickened and retracted. If spontaneous rupture has occurred, there is often a chronic discharge.

The situation is particularly serious when the disease is unilateral and when the patient is a child, as two-thirds or more of all such patients are. An adult who suffers from tinnitus, a sense of fulness in the ear, or an impairment of hearing is likely to seek medical aid promptly. A child is not unduly troubled by these symptoms, and even the most observant adults responsible for his care may overlook his deafness if it is unilateral. Bilateral deafness, of course, is unlikely to be overlooked, but unilateral deafness may not be noticed until the impairment has become irreversible.

8. Still another unfortunate consequence has resulted from the indiscriminate and inadequate use of the various antibiotics, particularly penicillin: The number of organisms sensitive to it is decreasing; the number of resistant organisms is steadily increasing, and so is the number of patients sensitized to it. Pulaski's[4] personal studies, and his comprehensive review of the literature, show that whereas originally some 95 per cent of all staphylococci were sensitive to penicillin, now almost 50 per cent are resistant. It is quite true that other broad-spectrum antibiotics have been developed, which can be used in the place of penicillin. They are still, however, considerably more expensive. Their use is associated with more side-effects. And it would surely be an egregious error to assume, granted their similar misuse, which is rapidly coming to pass, that resistance to them is not a logical future possibility.

It should be emphasized again that the situation which has come to pass cannot be attributed to any failure of antibiotic therapy per se. The explanation is the misuse and the inadequate use of these extremely valuable agents.

The majority of cases of otitis media, as already pointed out, do not require this form of therapy. Spontaneous recovery is the rule when suppuration is absent, and there is no shadow of reason for treating it with drugs which are expensive, which are often difficult to administer, which may give rise to various side-effects, some of them quite serious, and which may so sensitize the patient that when, in the future, there is real need for these agents, they are no longer effective.

The principles of correct antibiotic therapy are based on the use of the agent selected after laboratory testing (1) in sufficiently large dosages, (2) over sufficiently long periods of time to produce optimal concentrations at the site of the infection, and (3) the maintenance of these concentrations at this site until the organisms have been destroyed. The methods by which antibiotics are used in otitis media usually violate all of these principles. The dosage is usually small, frequently so small as to sensitize the patient without accomplishing destruction of the organism. If optimal concentrations are secured, they are seldom maintained for sufficiently long periods of time. It is doubtful, in fact, that they are ever secured at the site of infection, for as Butler[5] points out, it is difficult to envisage the meeting of the prime requirements of antibiotic therapy in such a region as the middle ear: The regional blood vessels are small. They deliver relatively small amounts of blood. They are readily susceptible to thrombosis. Finally, the pathologic process is inaccessible to concentrations of the antibiotic because it is, in effect, a localized abscess contained in a bony case. In other words, the physician who resorts to antibiotic therapy as the sole method of treatment in suppurative otitis media has completely lost sight of the fundamental surgical principle that the drainage of pus must be accomplished by surgical means.

The objective of all treatment is (1) to relieve symptoms, which the antibiotics usually accomplish in otitis media; (2) to eradicate infection, which they sometimes accomplish but which they frequently do not; and (3) to restore the normal physiology of the affected part, which they cannot accomplish in the presence of suppuration. I suggest that one reason why these facts are not generally realized is that patients

with otitis media are not usually followed up, in the utterly fallacious belief that penicillin is so potent that its mere administration will take care of anything that may happen.

MYRINGOTOMY VERSUS SPONTANEOUS RUPTURE OF THE TYMPANUM

In view of these facts, the question arises whether the position taken by some physicians is sound, that myringotomy is an outmoded operation because the antibiotics have taken its place. The very word, Deweese[6] says indignantly, is being dropped from the vocabulary of students and pediatricians. There is no more justification for this point of view than there is for the position that spontaneous rupture is equally as satisfactory as selective incision. It may relieve the symptoms, but there are at least three reasons why it is not conducive to favorable progress:

1. The favored location for drainage is inferior, for the reason, to speak colloquially, that the only way to empty a barrel is to make an opening in the bottom. Rupture usually takes place at the superior portion of the tympanum, and is frequently too small for satisfactory evacuation of the exudate, whether it be serous or suppurative. Anyone who doubts that statement has only to witness the flow of exudate which practically always follows incision of the posteroinferior quadrant after spontaneous rupture.

2. Granted that some drums rupture in a location favorable for healing, others do not. If the perforation is in Shrapnell's membrane, chronic suppuration may occur in the attic, with all the risk of extension of the disease to the labyrinth, lateral sinus, facial nerve and meninges.

3. Rupture is always caused by ischemic necrosis. It is therefore to be expected, because the pus must tunnel its way through layers of tissue, that the drum would be more scarred in spontaneous rupture than in a clean surgical incision.

As to what happens when antibiotic therapy is employed with myringotomy, I, like other physicians brought up on the fundamental principle that the presence of pus requires surgical drainage, will continue to believe that what wrought the improvement was the release of pressure and evacuation of exudate, and that the influence of the antibiotic was entirely secondary.

PRINCIPLES OF THERAPY

If one rejects the management of primary otitis media by the antibiotics, what policy is to be followed? I suggest that we return to the following first principles, beginning with the proviso that the physician who undertakes to treat middle ear disease must have a practical working knowledge of its anatomy and the anatomy of adjacent structures in the infant, the child and the adult. As Rutherford[7] says, in a particularly excellent article on this subject, the use of antibiotics has become so widespread that many young physicians actually have not been taught the art of cleansing the aural canal, of identifying pathologic changes in the typmanum, of distinguishing between suppurative and nonsuppurative disease, and of performing myringotomy when it is indicated. From personal experience I can testify to the damage heavy-handed physicians can accomplish in the mere act of cleansing the aural canal.

Treatment begins with cleansing the external ear of cerumen and debris, to permit an initial examination of the tympanum. The canal must be kept clean thereafter and open for inspection until the normal physiologic state is restored.

Pain is controlled by aspirin, codeine, or some similar agent, depending upon the necessities of the special case. Heat or cold may be used, depending upon which gives more relief. Neither has any effect on the pathologic process.

Ear drops are not indicated. If they are effective enough to control pain, they are likely to disguise the severity of the infection. This holds for both the old-time phenol and glycerine instillations and the modern proprietary preparations. If an ear is painful enough to require local applications, the indication is even stronger to suspect exudation and to arrange for inspection of the tympanic membrane by a physician capable of performing myringotomy.

In mild cases, no other therapy is needed except for attention to the underlying cause of the middle ear disease, which usually is a blocked eustachian tube. If blockage is caused by an upper respiratory infection, the nose and nasopharynx must be treated to prevent reinfection through the tube, which must be kept patent, for proper ventilation of the middle ear. Direct inflation with a catheter is the procedure of choice, but it is almost impossible in very young children, in whom one must rely on the Politzer method.

The local application of nose drops is falling into disfavor, and we are relying more and more upon vasoconstrictors by mouth. Occasionally, both routes of administration must be used. If blockage of the tube is caused by an allergic rhinitis, antihistaminic therapy should be instituted. If hypertrophied adenoids are responsible, they should be removed at an appropriate time. The general health of the child with otitis media should be maintained at the highest possible level.

Management of Suppurative Otitis Media.—In nonsuppurative disease of the middle ear, careful application of the regimen outlined will almost invariably control the infection promptly. In exudative disease, whether the exudate is serous or suppurative, more active treatment is necessary. Once middle ear disease is diagnosed, myringotomy is indicated under the following circumstances: (1) Severe and continuous pain. (2) Bulging of the tympanic membrane. (3) Loss or reduction of hearing in an acutely painful ear. (4) A high septic temperature not otherwise accounted for. (5) Headaches and pain in the mastoid area. (6) Convulsions in infants. (7) Spontaneous perforation with evidence of inadequate drainage.

Myringotomy should also be performed in all doubtful cases, whether or not the indications just listed are present. There is far less risk in incising the tympanic membrane unnecessarily than in allowing an undetected exudate to persist in the middle ear. There is also considerable merit in the contention of some authorities that if the physician suspects that a patient is unlikely to return for observation, there is all the more reason for performing paracentesis at once whenever it is thought that it might later be required.

Dry therapy is recommended after myringotomy in preference to the use of any solution or medication. The patient must be seen frequently, so that the ear can be cleansed with the suction tip or with dry sterile applicators. He should be shown, or his mother should be shown, how to insert dry cotton wicks to absorb drainage and how to change them before they become saturated. In all these maneuvers aseptic precautions must be observed and manipulations must be extremely gentle, to avoid damage to the tympanum and the introduction of secondary infection.

When the postoperative course is satisfactory, drainage is free and gradually changes from serosanguineous to purulent and then to mucoid. At the same time, the thickened, inflamed membrane becomes paler and thinner and reassumes its normal position. Under these circumstances there is no need for antibiotic therapy. If, however, there has been no marked improvement within twenty-four hours after myringotomy, if the temperature remains high, and if the patient seems toxic, then adjunct therapy is indicated. The particular antibiotic employed is selected according to the type of infection present. It must be given in adequate dosages, and over a sufficiently long period of time. Continuation of the infection is the inevitable result of violation of these principles.

These are clearcut indications for antibiotic therapy. It should not be used in their absence unless there is some equally clearcut indication for its use, such as follicular tonsillitis, pneumonia or rheumatic fever, or nephritis or diabetes in children.

THE STATISTICAL EVIDENCE FOR MYRINGOTOMY

In conclusion, I should like to cite certain statistics which are frankly selective but which I think are worth quoting because they are based on the comparison of like with like. To report and compare cases of otitis media merely as treated or not treated

with antibiotics is totally misleading in view of the fact, already several times emphasized, that this is a self-limited disease and that the great majority of cases will subside spontaneously under simple therapeutic measures.

Page,[8] in 1934, when there were no antibiotics, reported 18 mastoidectomies in 171 cases of middle ear disease. Ten were required in the 134 cases in which myringotomy was performed. Eight were required in the 37 cases in which rupture occurred spontaneously.

Hall,[9] in 1937, just at the beginning of the chemotherapeutic era, reported that of 221 patients submitted to myringotomy, only 28 required mastoidectomy, while of 189 patients who required mastoidectomy, only 28 had had paracentesis.

Butler,[5] in 1948, reported 461 cases of purulent otitis media treated in an army camp and therefore carefully followed up. Although neither chemotherapeutic nor antibiotic agents were used in any case in the series, only 2 patients required mastoidectomy.

Richardson,[10] in 1942, followed 625 patients with otitis media at the Massachusetts Eye and Ear Infirmary from puncture of the drum to complete healing. Only 5.3 per cent required mastoidectomy. Evans,[11] in 1951, reported two series of cases treated at the same institution during the April-July period in 1948. Forty-five patients with acute suppurative otitis media were treated in the outpatient clinic by early puncture supplemented, in a few instances, by chemotherapy. All made good recoveries. Of the 30 patients hospitalized with acute mastoiditis over the same period, all but 2 had been treated with antibiotic agents, usually in insufficient dosages and for brief periods of time, and not one had been submitted to myringotomy. Thirty-six mastoid operations were necessary in these 30 cases.

Rutherford,[7] in the excellent article previously referred to, reported 150 myringotomies performed in her private practice over a two-year period. Thirty-six of the patients had ruptured drums, with unsatisfactory drainage, when they were first seen. In every instance in the series recovery ensued, without recurrences or complications, within a range of four to fourteen days, and in most instances within six to nine days. One hundred and eight of the patients were treated without antibiotic therapy.

Deweese,[6] in discussing this paper, mentioned 26 patients with otitis media who came under his observation after they showed hearing losses. Only 4 patients in the group had been submitted to myringotomy. All the others had sustained spontaneous rupture, which in every instance appeared adequate for drainage but which in every instance left the child, after resolution of the infection, with some residual deafness.

There is no doubt that the incidence of surgical mastoidectomy in otitis media has been materially reduced in recent years. That this is entirely due to the use of the antibiotics seems highly doubtful. Over the same period methods of communication and transportation have improved, so that physicians and hospitals have become easier of access. Acute otitis media has itself decreased, a reduction which can be attributed to the use of the antibiotics in antecedent pneumonia and other severe respiratory infections. Furthermore, the virulence of otitis media varies widely from year to year, and the variety observed in recent years has been unusually mild. The physician who is tempted to attribute the encouraging recent developments in this disease to the widespread use of the antibiotics might bear these practical considerations in mind, and might reflect, also, upon the damage that is still being done by the unwise and indiscriminate use of these very valuable agents.

SUMMARY AND CONCLUSIONS

The widespread and indiscriminate use of antibiotic drugs in otitis media has led to a serious situation. Clinical improvement has masked continuing infection, and complications of various degrees of gravity have ensued. One of the most important is residual deafness. The cardinal surgical

principle that pus must be evacuated by surgical means has been all but forgotten, and myringotomy is omitted in many cases in which it is the essential treatment.

A therapeutic regimen, based on whether otitis media is suppurative or nonsuppurative, is outlined, and the indications for myringotomy are cited. The indications for antibiotic therapy in this disease are also stated.

Statistical evidence to show the value of myringotomy has been adduced.

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SOME PROBLEMS IN THE THERAPY OF AMEBIASIS*

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PREVALENCE

On the basis of many surveys of population groups it has been shown[1] that *Endamoeba histolytica* can be found in the feces of approximately 10 per cent of the population of the United States. Consideration of the technical methods involved in arriving at this estimate led Faust[2] to suggest that even this figure may be too low. Perhaps 20 per cent of the general population may be parasitized and in many poorly sanitated and primitive regions the incidence may be even higher. This prevalence of infection, particularly in the South, imposes a twofold responsibility on the physician. The first of these involves the prompt diagnosis of all infected individuals; the second necessitates recognition that the prevalence of amebiasis insures its frequent incidental occurrence with many unrelated disorders.

PRIMARY CLINICAL MANIFESTATIONS

It seems likely that the demonstration of *Endamoeba histolytica* in the feces of an individual means that his tissues have been invaded by the parasite.[3] While the validity of this concept has been questioned, there can be no doubt of the potentiality of parasitic invasion of host tissues whenever this parasite is demonstrated in the feces. When entry into the host tissue by *Endamoeba histolytica* occurs, it is invariably through the colonic mucosa. The favorite sites of colonic lesions are in areas where stasis of the fecal stream occurs; namely, in the cecum, the rectosigmoid and rectum, and the flexures of the colon.[1] These lesions vary from the most minute, unlikely to produce even minor colonic dysfunction, to such extensive destruction that one wonders how the organ is able to maintain its physical much less its functional integrity. Fortunately, the less extensive injury is more likely to occur. Regardless of the degree of colonic injury, the invading amebas may extend beyond the confines of the bowel to contiguous tissues or gain access to distant organs by way of the mesenteric blood vessels, and in both instances, produce serious extracolonic disease.

The colonic location of the primary lesion of amebiasis leads inescapably to the fact that the primary clinical manifestations of the disease are related to colonic dysfunction. And, these manifestations are related to mechanical injury of the organ.

*Presented at the Seventy-third Annual Meeting of the Louisiana State Medical Society, New Orleans, May 9, 1953.

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The symptomatology then of primary amebic disease is that of an irritable colon.

SYMPTOMS

Like the colonic lesions the symptoms of amebiasis can be most inconspicuous or most impressive. Usually, by employing appropriate and adequate methods of clinical examination including fecal analysis (microscopic, bacteriologic and chemical), sigmoidoscopic and radiographic examination, it is possible to show that the character and severity of the colonic symptoms are related to the nature, extent and location of the colonic lesions.

Experience indicates that less than 3 per cent of patients with amebiasis present frank dysenteric symptoms. The well known syndrome of the frequent passage of small mucosanguineous ("currant jelly") stools, accompanied by localized or generalized abdominal pain and tenderness and frequently by tenesmus is classical. In many such patients it is easy to demonstrate colonic lesions by sigmoidoscopic and radiographic examination, and the trophozoites of *Endamoeba histolytica* can be found readily by microscopic examination of the excreta. Fulminating rapidly fatal cases occur, but in temperate climates the average patient with acute dysenteric symptoms presents a remarkable paucity of systemic manifestations such as an impressive increase in body temperature, prostration, leukocytosis or anemia. The presence of these systemic manifestations should lead one to suspect the development of complicating factors. Occasionally the major inconvenience experienced by the patient is the frustrating necessity of remaining near a toilet. When long continued, the process will inevitably lead to exhaustion, dehydration, anemia, weight loss and other serious consequences resulting from chronic colonic disease. Unlikely as it seems, an occasional patient with neglected dysentery is still seen. The following is an illustration of such a patient.

A. B., a 60 year old white man, had suffered intermittent bouts of bloody diarrhea and asthma for some twenty years. His asthma had been well treated but little attention had been paid to the dysentery. A few days before admission to the hospital he became gravely ill with severe sanguineous rectal discharge. The patient died in shock a few hours after admission. The diagnosis of amebiasis was readily established at the time of admission by demonstration of trophozoites of *Endamoeba histolytica* in the bloody fecal material. Postmortem examination showed a short, markedly thickened colon. Extensive ulceration was present from the terminal ileum to the rectum. The colon was full of blood. Parasites were numerous in these tissues.

The larger group of patients infected with *Endamoeba histolytica* do not present frank dysentery and it is this group that constitutes the major problem of amebiasis. The symptoms described among these patients are varied and numerous. However, even in this group, frequently the symptomatology can be related by appropriate methods of investigation to the nature and extent of the colonic lesions. The symptoms definitely attributable to colonic amebiasis also result from colonic dysfunction, which may be manifested by localized or generalized abdominal pain of variable severity associated with the act of defecation. Constipation is frequent; episodic bouts of diarrhea and constipation may be prominent; and, rarely, severe watery diarrhea may be persistent. Many patients present no symptoms at all.

COMPLICATIONS

Serious complications are more likely to be encountered in frankly dysenteric amebiasis. The often inconspicuous symptoms of the non-dysenteric patient, however, do not eliminate the liability for developing the serious consequences of the disease. The percentage of the nondysenteric patients who develop these complications is small, but the prevalence of the infection assures the development of a number of these serious complications. In the absence of prominent colonic manifestations to direct attention to the possibility of amebic infection, many of these important complications go unrecognized. The key to their detection and proper assessment resides in always thinking of the possibility of amebic etiology. The following illustrates this point.

M. T., a 57 year old Negro, was admitted to the hospital with no antecedent history of colonic disorder. Approximately two months before admission he began to experience serious organic difficulty manifested by localized pain in the right up-

per quadrant of the abdomen, fever, chills and weight loss. Barium studies of the colon demonstrated a fistulous tract from the hepatic flexure of the colon and extraluminal barium in the subhepatic area. Cysts of *Endamoeba histolytica* in the feces and a positive complement fixation test for amebiasis suggested an amebic perforation of the colon with subhepatic abscess formation. Under treatment with emetine hydrochloride symptoms vanished and the fistulous tract disappeared. Following further treatment with intestinal amebacides, he has remained well for over a year since completion of therapy.

Another illustration of this point is presented by the following patient's record.

P. A. M., a 34 year old white man, had never had dysentery but had intermittent bouts of diarrhea and constipation and associated localized pain in the right lower quadrant of his abdomen. His appendix had been removed. His hospital admission was prompted by an attack of severe diarrhea, cramping and localized lower right quadrant pain. The stools showed cysts of *Endamoeba histolytica*. The cecum on radiographic examination presented a deformity which was interpreted to represent cecal involvement with amebiasis. The remainder of the colon was negative. Under treatment with emetine hydrochloride, 7-chloro-4-[4 diethylamino-1-methyl butylamino] quinoline (chloroquine), p-carbamino -phenylarsonic acid (carbarsone), and idoxy quinoline sulphonic acid (chiniofon), symptoms improved but the cecal deformity did not entirely disappear. The filling defect and extreme irritability were replaced by a deformity which probably represented scarring of this portion of the colon. Follow-up over the past four years has shown no recurrence of the amebiasis and aside from minor degrees of colonic dysfunction, this patient has remained well.

Perhaps this patient's record justifies the assumption that he had an amebic granuloma of the cecum. These granulomas which represent reparative exuberance on the part of the colon in response to the injury produced by *Endamoeba histolytica* can be demonstrated readily even in patients without serious dysenteric symptoms. A few years ago Silverman and Leslie[4] called attention to the necessity for differentiating these lesions from malignant diseases of the bowel. Favorite sites for the development of these granulomas are in the cecum and in the rectum but they may occur anywhere in the bowel. When the lesions are located in the rectum and the lower sigmoid, biopsy is the only sure method of differentiation of these lesions from carcinoma. The presence of a filling defect in the cecum or elsewhere on radiogdaphic examination in the presence of amebiasis suggests a granuloma, but absolute differentiation without biopsy is impossible. A therapeutic trial with emetine hydrochloride and careful observation of the patient may be employed but in many instances direct surgical approach is required. The following case illustrates the necessity for care in making the assumption that a cecal radiographic defect is owing to the presence of an amebic granuloma even in the presence of amebiasis.

J. A. B., a 41 year old white man, was hospitalized because of fatigue and weakness. There were minimal symptoms of bowel disturbance. The stools were always soft and mushy and occasionally there were bouts of diarrhea. Radiologic examination showed a filling defect in the cecum. Laboratory examinations demonstrated a profound anemia. Trophozoites of *Endamoeba histolytica* were numerous in the feces. A therapeutic trial with emetine hydrochloride had no effect on this lesion. At exploration a colloid carcinoma of the cecum was found. Amebae were demonstrated in the exudate over the carcinoma and in the bowel wall elsewhere.

Of more importance because of the gravity of the complication is the disease produced in distant organs which are invaded by *Endamoeba histolytica*. This is particularly true when the colonic manifestations of the disease are either absent or insignificant. The most frequent complication of this type encountered is, of course, the amebic hepatic abscess. DePakey and Ochsner[5] in their survey of 263 cases of amebic abscess of the liver call attention to the fact that the paucity of colonic manifestations in the presence of frank amebic hepatic abscess has been insufficiently emphasized. Criteria for establishing a diagnosis of amebic hepatic abscess are definite. The important aspect in the problem is that it should always be thought of in the presence of right upper quadrant abdominal and/or lower right lung signs and symptoms, even in the absence of colonic dysfunction. Experience in the past seven years with 47 patients with amebic hepatic abscess who have been hospitalized has shown that few of them have been diag-

nosed prior to hospitalization. Valuable time and therapy is wasted, primarily, because an amebic complication is not considered. The illnesses of these patients have masqueraded as a variety of diseases such as pneumonia, gallbladder disease, cholangitis, coronary thrombosis, heart failure, and tumors of the liver. The folowing patient's record will serve to illustrate some of the difficulties in making the diagnosis of amebic hepatic abscess and the serious consequences which result from the disease.

G. M., a 38 year old white man, came to the hospital with chills, fever, and pain in the right upper quadrant of the abdomen. The physician who sent him to the hospital thought that he had malaria. No parasites were found in the blood and many studies failed to demonstrate a specific cause for his fever. Careful questioning failed to produce any symptoms of colonic disorder. The exquisite right upper quadrant pain and elevated and paralyzed right diaphragm led to a working diagnosis of a hepatic abscess. An extraperitoneal exploration of the liver was performed. Inspissated creamy pus was obtained from numerous small abscesses in the right lobe of the liver. This pus was sterile and no amebas were found. The possibility of an amebic hepatitis was considered at this time and a course of 12 grains of emetine hydrochloride was given. His signs and symptoms of disease in the right upper quadrant diminshed coincident with the surgery and the administration of emetine hydrochloride. Because of the multiplicity of the small abscesses and the presence of creamy pus it was felt that the best diagnosis was that of a suppurative cholangitis.

One month after his discharge he again developed fever, cough, pain in the right upper quadrant and at this time associated with right shoulder tip pain. Radiographic and fluoroscopic examination again showed elevation and paralysis of the right diaphragm. Cysts of *Endamoeba histolytica* were demonstrated in the stools on this occasion and it was felt certain at this time that this patient had an amebic abscess of the liver. After a preliminary twelve-day course of emetine hydrochloride, needle aspiration of the liver was undertaken. Creamy pus in small amounts was aspirated but because of the continuing encroachment of the abscess on the right lung and the failure of aspiration to evacuate the abscess, it was decided to drain this patient surgically. Through an extraperitoneal surgical approach a large solitary abscess containing much creamy pus was evacuated. *Endamoeba histolytica* trophozoites were subsequently found in the discharge from the draining sinus. The abdominal wall about the sinus became necrotic; the process extended into the pleural cavity; a bronchopleural fistula developed; and despite repeated but probably inadequate courses of therapy, death occurred about five months after admission. At postmortem examination, in addition to the lesions previously mentioned, an amebic abscess of the brain was demonstrated.

PERSISTENCE OF SYMPTOMS

In contradistinction to those patients illustrated in the foregoing portion of this paper whose symptoms can be related to organic changes, there are a large number in whom symptomatology is far more impressive than any demonstrable organ damage. In addition to the colonic manifestations many of these patients exhibit a wonderful number of nonspecific complaints. Anorexia, nausea, pyrosis, headache, weight loss, arthritic pains, lack of ambition, impotence, chronic fatigue, inability to concentrate, somnolence and insomnia, as well as various vasomotor disturbances (excessive sweating, flushing, dermographism, bradycardia and tachycardia) have all been attributed to infection with *Endamoeba histolytica*. These general symptoms are difficut to relate to the presence of injury to the colon which to a greater or less degree is presumed to exist in patients with amebiasis. A most distressing feature is the large number of these individuals who fail to obtain symptomatic relief after successful antiamebic therapy.

Following the acute dysenteric form of amebiasis in which definite colonic lesions can be demonstrated, not infrequently, some patients present residual symptoms or recurrences of symptoms which defy explanation. This persistence of symptoms in the patients with and without demonstrable structural lesions in the colon or elsewhere is a serious problem in therapeusis. The lack of successful relief of symptoms leads to the necessity of inquiry into the reasons for their persistence.

In the following discussion of the reasons why symptoms may persist after successful treatment of amebiasis, it is presumed that certain proprieties in making a diagnosis of the initial infection, a relapse or reinfection with *Endamoeba histolytica* have been observed. It is perfectly obvious that a mistake in diagnosis will lead to fruitless therapy. Many misdiagnoses of amebic disease

are based upon misidentification of certain harmless coprophages. The ones commonly found in the stool are *Endamoeba coli, Endolimax nana, Iodamoeba buetschlii* and *Diendamoeba fragilis*. Frequently mistaken for cysts of *Endamoeba histolytica* are such artefacts as macrophages, yeasts and *Blastocystis hominis*. Of equal importance to the recognition of these various confusing elements is the necessity of adequate examinations to determine the presence of *Endamoeba histolytica*. This requires multiple stool examinations before and after purgation, the employment of stool concentration techniques (we have preferred the zinc sulfate centrifugal flotation method), the resort to microscopic examination of material directly aspirated from the bowel or scrapings of the colonic mucosa obtained during sigmoidoscopic examination when necessary. When identification of a suspicious object is in question resort to cultural and special staining techniques may be required.

Recurrences of amebic infection after treatment do occur, it is true, and account for recurrent symptoms but should be diagnosed only on the basis of demonstration of the causative organism in the feces. Most reports.[6, 7, 8] of patients treated with antiamebic drugs, currently popular, indicate that the cure rate is high and relapse rate low. Our own experience agrees with these reports. Consequently our inquiries must be directed elsewhere to account for the large number of patients with symptomatic relapses in the absence of demonstration of the parasitic infection.

Another explanation for persistent or recurrent symptoms after successful antiamebic therapy is that the colon has been so severely injured by the amebic infection that it is unable to perform its normal function. Such a colon is that of A. B. presented earlier.

It was pointed out earlier that amebic infection will occur coincident with many other unrelated affections. Diagnostic surveys of patients who have had persistent symptoms after eradication of *Endamoeba histolytica* have shown that the symptoms could be related better to the presence of other concomitant diseases than to a nondemonstrable relapse of the parasitic infection. Encountered in these surveys have been malignant disease of the colon, diverticulitis, nonspecific ulcerative colitis, cicatrizing stenosing enterocolitis (Chron's disease), strongyloidiasis, relapsing pancreatitis and a host of other disorders. A similar experience with persistent symptoms following treatment for amebiasis was recently reported by Dowdell, Roth and Shumway.[9]

A 40 year old white man had persistent episodic attacks of lower left quadrant pain and nonbloody diarrhea following successful treatment of amebic dysentery. Many studies indicated the absence of amebiasis and investigation of the colon showed a marked diverticulitis in the rectosigmoid area of the colon to account for these episodic recurrences.

PSYCHOSOMATIC FACTORS

It is well to remember that it is not always justifiable to assume that because *Endamoeba histolytica* can be found in the stools that all symptoms which a patient has are related to this infection even though it is probable that such a demonstration does indicate that at least the superficial layers of the intestine have been invaded. This is particularly true with regard to the nonspecific symptoms which are detailed above. It is probable even that constipation, alternating constipation and diarrhea, or persistent diarrhea, may not in every instance be owing to the presence of the parasite. The important demonstration of this fact resides in the failure to relieve symptoms by effective therapy. Many patients of this sort have been treated and retreated many times over a period of years with or without the demonstration of a parasitological recurrence. Such persistence with therapy, many times directed at a nonexistent etiologic agent, is frequently harmful.

As an approach to this aspect of the problem a study[10] of a small group of individuals by means of projective psychologic and interview techniques demonstrated that some of these patients are indistinguishable, on the basis of diagnostic criteria used, from a group of dependent neurotics. Our studies are not sufficiently large to justify

sweeping conclusions, but they do indicate that this is a fruitful line of approach to this vexing problem. The readiness with which patients in this group accept the diagnosis of amebiasis and the avidity which they cling to it through repetitious courses of therapy which do not relieve symptoms can be taken as support of the hypothesis that at least a part of the symptomatology is personality conditioned. An organic diagnosis furnishes to these patients a ready explanation for all personal inadequacies and failures. And like all dependent neurotics it relieves them of any personal responsibility in regaining their health. In their failures they frequently resort to the well known infantile pattern of under-production or over-production of feces, perhaps as a symbolic substitute for accomplishment. The other symptoms are well known features of somatization reactions.

This type patient is exemplified by the young lawyer who develops diarrhea and weakness on almost every occasion he has to go to trial. His disease is incapacitating and has almost impoverished him. Early demonstrable amebiasis has disappeared but his pattern of behavior still exists.

Another example is found in a radio station operator who had amebiasis and whose weakness, fatigue, and recurrent episodes of diarrhea in the face of business stress has necessitated transacting most of his business from bed even though no organic basis for this disability can be determined.

Still another example is a 31 year old salesman who had amebiasis but whose somatic preoccupations at the present time do not permit a successful pursuit of his business.

Therapy in these patients is difficult since the symptoms may be based in deep-seated personality disorders, but in many instances the physician can, with reassurance, encouragement, and education, give the patient some insight into the mechanism by which his symptoms are produced. Occasionally, some of his patients may be able to function efficiently and achieve a fair amount of happiness in spite of symptoms.

Nothing in the foregoing should be interpreted as indicating that patients without obvious mechanisms for production of their symptoms in the presence of amebic infection, should be neglected in terms of vigorous pursuit of therapy to the point of eradication of the parasite. The suggestion is being made only that when adequate therapy has eliminated the parasitic infection, recurrent symptoms need not depend upon an undiscoverable recurrent infection. It should be remembered that recurrences of amebiasis are no more difficult to diagnose parasitologically than the initial infection. When other causes exist, including non-organic ones, appropriate therapy may be more gratifying than the persistent pursuit of antiamebic therapy.

It is necessary to make a brief comment about adequate therapy. Recent reports have indicated the efficacy of certain antibiotics, particularly oxytetracycline ("terramycin") in intestinal amebiasis with which our own experience is in agreement. The exhibition of this agent in extracolonic amebiasis is noneffective and may result in disastrous consequences as illustrated by the following.

A 65 year old white man had chills and fever for 3 weeks. Treatment with penicillin, aureomycin and sulfonamide drugs in unknown amounts had no beneficial effect. During the 10 days prior to his death 15 grams of oxytetracycline ("terramycin") were administered and at autopsy a huge amebic abscess of the liver was found as well as a granuloma of the cecum. Each of these contained easily demonstrable trophozoites of *Endamoeba histolytica*.

When extracolonic complications are present or suspected, adequate therapy with emetine hydrochloride and/or 7-chloro-4-[4 diethylamino-1-methyl butylamino] quinoline (chloroquine) should be employed always. These two drugs, while extremely effective in extracolonic amebiasis, are relatively noneffective colonic amebacides. The administration of an effective intestinal amebacide should always follow or accompany therapy with either of these. Therapy should be pursued to the point of eradication of the parasite. The drugs which we have employed effectively have been: 5,7-diiodo - 8 - hydroxyquinoline (diodoquin);

iodoxy-quinoline sulphonic acid (chiniofon); p-carbamino-phenylarsonic acid (carbarsone); bismuth glycolylarsanilate ("milibis"); and oxytetracycline ("terramycin").

SUMMARY

The high incidence of amebiasis and the likelihood of its occurring coincident with nonrelated affections has been discussed.

The primary manifestations of amebic disease are colonic in origin, and in many instances appropriate study will relate the colonic injury to the clinical symptomatology. Occasionally complications which include extracolonic manifestations of amebic disease will occur. The key to their recognition is to suspect them even when the colonic aspects of the disease are absent or inconspicuous.

An important complication of amebiasis is the persistence of symptoms following treatment, which may be owing to recurrent infection, rarely to extensive injury of the colon, more frequently to concomitant other organic disease, and sometimes related to a personality conditioned somatic response. Adequate therapy of both the amebic infection and concomitant disorders, either organic or psychic, is required for the successful management of these patients.

Therapeutic agents so effective in the treatment of intestinal amebiasis, including antibiotics, are ineffective in the treatment of extracolonic amebic disease. The extracolonic amebic lesions should be treated with adequate amounts of 7-chloro-4-[4 diethylamino-1- methyl butylamino] quinoline (chloroquine) and/or emetine hydrochloride first, and in every instance adequate treatment with an effective intestinal amebacide should follow.

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EOSINOPHILIA IN CHILDHOOD CAUSED BY VISCERAL LARVA MIGRANS*

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NEW ORLEANS

INTRODUCTION

In a previous publication,[1] a syndrome designated as visceral larva migrans was described, and some of the salient features of its pathogenesis and pathology were discussed. This term was chosen because it denotes the aimless migration of the larvae of certain round worms through the human viscera, although the particular species in question is not a definitive parasite of man. In that study, the finding of a larva of *Toxocara canis*, the dog ascarid, in a liver biopsy of one of three children with similar symptomatology, clinical history, and peripheral blood eosinophilia, led to the postulation of a likely explanation for this syndrome; namely, that the etiologic agent is probably the larval stage of nematodes usually parasitic in lower animals but which are capable of invading and damaging the human tissues and stimulating an eosinophilic response in the circulating blood. The condition is the visceral counterpart of the well known entity cutaneous larva migrans in which skin penetrating larvae of certain hookworms produce typical dermatological lesions.

The cosmopolitan distribution of *Toxocara canis*, and the close association of children with dogs, immediately suggested that this type of atypical parasitism may be relatively frequent and that it may, in fact, ac-

*Presented at the Seventy-third Annual Meeting of the Louisiana State Medical Society, at New Orleans, May 9, 1953.

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count for numerous cases of chronic eosinophilia in children. A careful study of the clinical and pathologic material at hand has borne out this original supposition.

Because chronic eosinophilia is a prime feature of this syndrome, it is pertinent to discuss it at this point. An elevated eosinophil count in the peripheral blood is a fairly common finding in an active pediatric practice and one which is often difficult to explain. More frequently than not, eosinophilia comes as a distinct surprise to the clinician when it is discovered on routine blood studies. Often, extensive clinical and laboratory investigations may fail to disclose any adequate explanation of the eosinophilia.

Some generalizations concerning the behavior of the eosinophil are well established. For example, the total number of circulating eosinophils decreases spontaneously at the onset of most acute infections and in time of stress. Recently, considerable interest has been aroused by the artificial depression of the circulating eosinophils using adrenal steroids and corticotropins. The specific functions of the eosinophil still remain a mystery.

Numerous diseases, apparently unrelated, are characterized by eosinophilia. (See Table 1) A consideration of the causes listed, reveals the fact that the most pronounced eosinophilias occur in infections with animal parasites which are actual tissue invaders.

TABLE 1

CAUSES OF EOSINOPHILIA

	Disease	Degree of Eosinophilia
1.	*Allergic Disorders*	Slight to moderate
	Bronchial asthma	
	Urticaria	
	Hay fever	
2.	*Skin Diseases*	Slight to moderate
	Phemphigus	
	Exfoliative dermatitis	
	Dermatitis venenata	
3.	*Certain Infections*	Slight to moderate
	Scarlet fever	
4.	*Hodgkin's Disease*	Slight to moderate
5.	*Miscellaneous Diseases*	Slight to moderate
	Sydenham's chorea	
	Erythema multiforme	
6.	*Parasitic Infections*	Moderate to severe
	Trichiniasis	
	Schistosomiasis	
	Filariasis	
	Ancylostomiasis	
	Strongiloidiasis	
	Ascariasis	
	Visceral Larva Migrans	Moderate to severe

CLINICAL OBSERVATIONS

Our direct knowledge of visceral larva migrans is derived in part from 7 clinical cases† with 2 confirmatory liver biopsies and 1 complete autopsy,‡ and in part from material submitted for consultation from 3 other cases in which a specific diagnosis has been established, and 3 additional cases in which the larvae have not been identified, but which showed typical histologic lesions.

In our experience, visceral larva migrans occurs in young children, usually from 18 months to 6 years of age—an age range within which children are most likely to swallow dirt. The symptoms are protean and consist of intermittent fever, malaise, pallor, loss of appetite, irritability, failure to gain weight, and muscle aches and pains. The children in our series have been "dirt-eaters" and there has been close association with pets, especially dogs. Early in the illness, a distressing cough may be present for several weeks. In most of our cases, there has been an impetiginous type of skin rash that is confined principally to the trunk and lower extremities, and which consists of small intensely pruritic ulcerated areas. Bouts of nausea and vomiting generally accompany the febrile episodes. These episodes usually last from a week to ten days, with a daily elevation of temperature to about 105° F. The temperature subsides by lysis. During the next week or two the patient may show an occasional moderate rise in temperature up to about 103° F. There is a tachycardia in proportion to the elevated temperature. The patient appears to be extremely languid. Examination of

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‡To be reported in detail elsewhere.

the sclerae may reveal a slight degree of jaundice. The liver and spleen may be enlarged, and some abdominal distention is usually present. Examination of the chest may reveal findings suggestive of a bronchitis or even a bronchopneumonia. X-ray studies of the chest at this time will usually reveal diffuse patchy areas of pneumonitis, suggesting a bronchopneumonia, and even, in some instances may resemble miliary tuberculosis. Frequently, the test for occult blood in the stools has been reported positive. Examination of the blood has always shown a marked eosinophilic leukocytosis in all our patients, the total leukocyte count ranging from 15,000 to 80,000 cells per cu. mm. with an eosinophilia which fluctuates between 30 per cent to 80 per cent at different times even in the same patient. Most of the eosinophils are mature, although eosinophilic myelocytes are often encountered. A normocytic hypochromic anemia is the rule. The degree of anemia parallels closely the severity of the systemic symptoms. The anemia is somewhat refractory to treatment, but generally a reticulocyte response will be noticed following the administration of therapeutic amounts of iron. The bleeding and coagulation times and the sedimentation rate are usually within normal limits. In two cases a marked increase in the number of platelets in the peripheral blood was noticed and in one of these hyperplasia of the megakaryocytes of the bone marrow was found.

Frequently, children who present the above clinical picture reveal behavior disorders and are emotionally unstable. One patient, during the height of the illness presented symptoms identical with those of petit mal. This episode of petit mal lasted only a few weeks, and has not recurred after a period of approximately two years. Neurological examinations and eyeground studies have yielded no essential information. In one case which died and came to autopsy, the larvae of *T. canis* were recovered from crushed preparations of brain tissue. Histologic study of sections of this child's brain showed numerous glial nodules, presumably along the paths of the larvae. This case suggests that more careful consideration should be given to the cerebral manifestations and the emotional and behavior disorders of these children.

The clinical picture described above corresponds to massive infections with these vigorous larvae. Just as striking, and more difficult of explanation, is the apparently healthy child who reveals nothing abnormal except a rather pronounced eosinophilia and a mild hypochromic normocytic anemia. Generally, these children have no specific complaints other than frequent and severe bouts of "bronchitis." The growth and development in both categories is not markedly abnormal. A probable explanation for the protean symptomatology lies in the fact that as far as is known, these larvae are able to penetrate and live for some time within any soft tissue or organ of the body. Apparently, the degree of eosinophilia reflects, in a broad sense, the quantitative aspect of the parasitic infection and the concomitant allergic response of the host. A study of our cases indicates that the more prolonged and massive infections are likely to show the highest eosinophilias and the most pronounced symptomatology; whereas, relatively light infections may be manifested only by an eosinophilia. The eosinophilia of the peripheral blood has been found to be a reflection of a similar response in the bone marrow.

PATHOGENESIS

Embryonated eggs are usually found in moist dirt contaminated with dog's feces. After being swallowed by the child, the larvae hatch and penetrate the mucosa of the small intestine in a matter of hours. Migration, believed to be by way of the portal blood, the lymphatics, and the tissue spaces, then starts. Most larvae go to the liver where they rupture sinusoids and hepatic cell cords, breaking the reticulum fibers and producing along their tracts, areas of necrosis and hemorrhage. The larvae move backwards as well as forwards, with twisting serpentine motion. Those that by-pass the liver may reach the lungs by way of the pulmonary arteries, although direct migration through the tissues is also a possibility.

Once in the lungs, they may either penetrate the bronchial tree to go up the trachea and be swallowed again, or go by the pulmonary veins to the heart and the systemic circulation to any other organ or tissue in the body. Those that are reswallowed, presumably penetrate the intestine once more and repeat the migratory pathways.[2] Larvae of *Toxocara canis* may live in abnormal host's tissues for months but are eventually encapsulated by host's fibrous tissue and die. Figures 1 and 2 show the differences be-

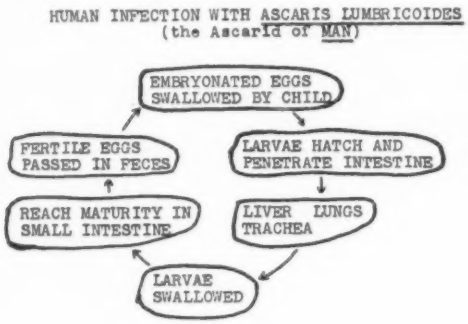
HUMAN INFECTION WITH ASCARIS LUMBRICOIDES
(the Ascarid of MAN)
EMBRYONATED EGGS SWALLOWED BY CHILD
LARVAE HATCH AND PENETRATE INTESTINE
LIVER LUNGS TRACHEA
LARVAE SWALLOWED
REACH MATURITY IN SMALL INTESTINE
FERTILE EGGS PASSED IN FECES

Figure 1

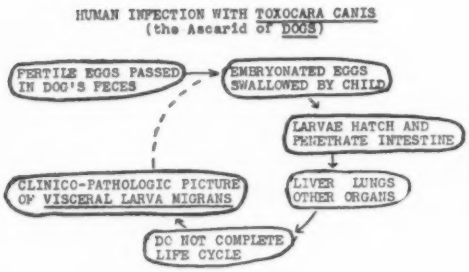
HUMAN INFECTION WITH TOXOCARA CANIS
(the Ascarid of DOGS)
FERTILE EGGS PASSED IN DOG'S FECES
EMBRYONATED EGGS SWALLOWED BY CHILD
LARVAE HATCH AND PENETRATE INTESTINE
LIVER LUNGS OTHER ORGANS
CLINICO-PATHOLOGIC PICTURE OF VISCERAL LARVA MIGRANS
DO NOT COMPLETE LIFE CYCLE

Figure 2

tween human infection with *Ascaris lumbricoides* and *Toxocara canis*. It is important to observe that while infection with *Ascaris lumbricoides* can eventually be diagnosed by parasitological examination of the feces, for the ova or the adult worms, no such thing is possible in the case of infection with *Toxocara canis*, in which the worms never exist in the human intestine as egg-laying adults and hence parasitological examination of the feces is necessarily non-informative.

PATHOLOGY

Lesions produced by the larvae of *T. canis* may occur in the various organs or tissues to which they migrate and have been observed, so far, in liver, lungs, brain and kidney. Most of the lesions, in our cases, occurred in the liver and lungs, which are the first natural barriers in the larval migratory pathway. In the organs in which the parasites were found at autopsy, as well as in the liver biopsies, the larvae and their tracts are surrounded by a variable granulomatous inflammatory reaction apparently depending, in character and intensity, on the age of the lesion and the specific host tissue reactivity. The early lesions consist of a central zone of tissue destruction surrounded by inflammatory cells, mostly eosinophils and neutrophils. A larva may or may not be present at a given level of the tortuous tract, but when present, it usually occupies a central position in the area of necrosis if observed in cross section, but if followed in serial sections its position is almost invariably at the advancing end of the tract. Thus, it is apparent that one larva, because of its continuous active movements, may be responsible for a great deal of tissue destruction. Since the larvae move away from the lesions which they constantly produce, it is not surprising that they are difficult to find in biopsy material except when meticulously searched for in numerous serial sections. The older lesions, or those around degenerating larvae, show, in addition, large foreign body giant cells, epithelioid cells, macrophages and lymphocytes around the central area of necrosis. Charcot-Leyden crystals have been observed in some lesions. A peculiar eosinophilic fibrinoid material is occasionally observed radiating from the necrotic center of the lesions. Figures 3 and 4 show the morphologic appearance of the larvae as seen in tissue sections, and the character of the tissue reaction. A detailed study of the morphology of the larval stage of *T. canis* has been recently done at Tulane University by Nichols.[3]

PROGNOSIS

The ultimate prognosis is good in most cases. The parasites, however, may remain active and the patient continue to be symptomatic for months. As already indicated,

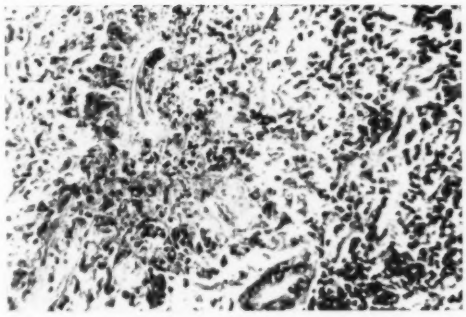

Figure 3. Anterior end of *T. canis* larva in granulomatous lesion of liver. (H & E Ca. 220 x).

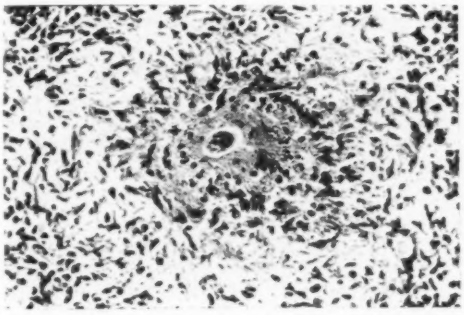

Figure 4. Cross section through midportion of *T. canis* larva surrounded by epitheloid cells, leukocytes, and fibroblasts. This lesion is probably older than that seen in figure 3 (H & E Ca. 220 x).

the morbidity is probably directly proportional to the number of ova ingested. The continued ingestion of heavily polluted soil by "dirt-eating" children results in a massive infection, and the final outcome may even be fatal, although in the cases we have known there has always been some other factor that precipitated death terminally. Even children with massive infections may be expected to recover, if the source of contamination is removed. It is conceivable, judging from the character of the tissue damage, that irreversible changes may be produced in certain organs. Not enough is known about the central nervous system lesions to warrant speculation about their probable significance.

DIAGNOSIS

Since "dirt-eating" children are apt to ingest ova of other and more familiar parasites as well, the presence of infections with ascaris, whipworm, or pinworm, for example, should not be taken as the specific explanation for a chronic eosinophilia of high level. Mixed infections are the rule. On the other hand, the failure to find parasitic ova in the stools does not rule out visceral larva migrans due to *Toxocara canis or* to some other similar parasite of lower animals whose larva is a potential invader of human tissue, but which will not complete its life cycle and mature in man, an abnormal host. The failure to find parasitic ova in the stools of such patients has led, in the past, to such diagnoses as Loeffler's syndrome and tropical eosinophilia. Even more suggestive is the fact that when several children of the same family all have eosinophilia which cannot be accounted for, the term "familial eosinophilia" is the usual diagnosis. In two of the families of children with positive liver biopsy the siblings also had eosinophilia. If these two children had not had severe enough infections to warrant liver biopsies in search for the cause of their illness, familial eosinophilia would have sufficed as a reasonable explanation.

The pulmonary manifestations are clinically indistinguishable from those of Loeffler's syndrome and tropical eosinophilia.

The diagnosis must, of necessity, be clinical if there is a suggestive history, compatible physical findings, and chronic sustained eosinophilia that cannot be readily explained otherwise. No skin or serologic tests are as yet available.

Liver biopsy, when justified, may be the only means of establishing a definitive specific diagnosis by the finding and identification of the larvae. This may prove to be, as it has been in all our cases, a tedious and time - consuming procedure and one for which a highly qualified helminthologist must be available for the actual species identification of the larvae. Examination of crushed or partially digested fresh tissue and of stained serial sections may be necessary.

The gross appearance of the heavily infected liver at laparotomy is highly characteristic. The capsule is smooth and glistening and the organ is markedly congested. Against this dark reddish purple background, numerous discrete white areas from

pinpoint to 1 to 2 mm. in diameter are strikingly visible. Liver biopsy should consist of an ample portion, at least 1 or 2 centimeters in main dimension.

TREATMENT

There is, as yet, no specific treatment. In our cases, vitamins, iron, and short courses of antibiotics have helped symptomatically. Cortisone will usually ameliorate the symptoms and cause a temporary decrease in the absolute and relative numbers of circulating eosinophils. Hetrazan has been used in large doses without demonstrable permanent beneficial effects. Arsenicals, which are said to produce good results in tropical eosinophilia, have not been tried by us, but should be worthy of consideration in the future.

It is imperative, of course, to isolate the child from contaminated pets and polluted soil in which it is impossible, from a practical standpoint, to kill the ova. The treatment of infected animals should be done in cooperation with a veterinarian, but when absolute control is doubtful, animals should be barred from the household and extreme care should be taken to avoid contamination of yards and play rooms by strays or neighbor's animals or pets.

SUMMARY AND CONCLUSIONS

When the cause of eosinophilia in children cannot be specifically accounted for by well known etiologic factors, such as allergy or orthodox parasites, one must consider the possibility of visceral larva migrans caused by some species of nematodes normally parasitic in lower animals. It is suggested that the larvae of *Toxocara canis*, the ascarid of dogs, is probably the chief offender. Children become infected by swallowing dirt contaminated with feces of a worm-bearing dog, frequently his own pet. The larval parasites, after penetrating the intestinal mucosa, migrate through the organs and tissues, producing typical lesions and stimulating pronounced eosinophilia of the bone marrow and peripheral blood. Since thes larvae do not complete their life cycle in man, an abnormal host for them, egg-laying adult worms of this species are not to be found in the human intestine, therefore the specific diagnosis cannot be made by fecal examination. Liver biopsy is, at present, the only means of establishing the exact diagnosis. As yet, no specific treatment is available. Awareness of the mode of infection, with adequate prophylaxis against subsequent exposures is the best form of therapy, allowing the patient to outlive the present infection.

The syndrome of visceral larva migrans is presented as a problem of considerable moment to physicians, veterinarians, and public health officials, as well as to parents and children.

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ADVANTAGES OF A STATE SYSTEM FOR MEDICOLEGAL INVESTIGATION*

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NEW ORLEANS

The earliest records of activity of a coroner date to the twelfth century in England. The coroner at that time was a knight of high position whose chief duties were somewhat like a treasurer and tax collector. He was concerned with the properties of the king, to see that the taxes were collected, and that the king obtained his share of royal fish and whales that were swept up on the coast, and other such duties. Inasmuch as the people were subjects or property of the king, the death of a subject meant the loss of property to the crown, and it soon became the duty of the coroner to investigate the nature of deaths. It should be noted that in those early times, before the advent of scientific medicine, that the coroner was probably as well qualified as anyone else to render opinions as to the

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*Presented at the Seventy-third Annual Meeting of the Louisiana State Medical Society, at New Orleans, May 9, 1953.

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causes of death. In fact, he was probably one of the best qualified, for the number of educated was very small and he belonged to that select group.

With the advent of scientific medicine, the development of gross and microscopic pathology and chemistry during the nineteenth century, more specialized information was obtainable as to the causes of death. At about this same period, the means of committing crimes became more complex and intricate. And along with these new developments, that is, scientific medicine and scientific crime, there arose on the continent particularly in Germany and France and equally well in England, the science of medicolegal investigation. This field, a true medical subspecialty, achieved great prestige in Europe because of its many accomplishments but has only recently come to be recognized in this country. It is appalling to think that in this country at the present time in some thirty-six states, coroners may be, and most frequently are, lay people with no medical training, elected on purely political grounds. In other states, such as this one, the most important single stride in the improvement of medicolegal investigation has been taken; that is, to require that the coroner is of necessity a medical man. In some seven states at the present time there is a nonpolitical system in which individuals trained in this medical subspecialty conduct investigations into the causes and manner of death. The author has had experience working in states and doing medicolegal investigation under all three of these systems. The following remarks are based on his personal thoughts concerning the advantages and disadvantages of each system.

DISADVANTAGES OF LAY CORONERS

There is no need for me to point out in great detail to this group the disadvantages of a system employing lay coroners and inquests for the determination of the causes of death in cases requiring investigation. Medical diagnosis on the live patient is a difficult procedure under even the best circumstances. In only the most flagrantly obvious cases is the cause of death apparent from external inspection and we all know that even cases that appear obvious from external inspection often present quite different findings when complete examination is carried out. For a lay person to superficially examine a dead body and pronounce that the cause of death is due to a heart attack is like buying a pig in a poke. Equally ridiculous is the inquest where a lay jury is summoned for the purpose of determining the cause and manner of death. It would be equally wise to go out on the street and pick up the first ten people as a jury and bring them in to ask them whether an operation for appendicitis should or should not be conducted. Some may argue that in some such jurisdictions the lay coroner summons help in the form of consultants and orders autopsies. It should be pointed out that the great drawback of this system is that the important decision is whether the autopsy shall or shall not be performed and this decision is made by a lay person who cannot and has not been trained to evaluate medical histories or physical findings. As a result the type of cases that come to autopsy in such a jurisdiction are the obvious ones that have bullet wounds of the head or a knife sticking out of the chest. It can truly be said if one would get away with murder one should go to a state where a lay coroner operates.

Here in Louisiana the most important step in the improvement of medicolegal investigation has been taken by the passage of a law which requires the medicolegal investigator to be a medical man. Equally important are the features of the law that define accurately and broadly what are the types of cases to be investigated and give to the coroner complete discretion as to the type of investigation that should be carried out under his jurisdiction. In my short experience here the conduct of medicolegal investigation in, let us say, the Parish of Orleans approaches that of many of the better jurisdictions throughout this country and I am sure, having traveled around the state, that similar high type of medicolegal investigation is carried out in many of the other parishes. Despite the great advances that have been made in the system in Louis-

iana several features of the system stand out to me as being deficient and in need of reform.

DISADVANTAGES IN LOUISIANA SYSTEM

The first great drawback to be observed in the Louisiana Coroner's system is that the coroner is an elected official. This immediately means that for election he must be a politically astute individual and that his qualifications for office are therefore not necessarily based on ability and training in the field of medicolegal investigation but are largely based on political connections. We all are familiar with the adage that "politics and medicine do not mix" and I think that this expression is equally as applicable to this portion of medical practice as it is, let us say, to the practice of surgery.

Once in office, the politically elected coroner is beholden to certain individuals or groups for the support he has had from them in obtaining his office. He is constantly subjected to pressures of individuals who have friends who know someone who knows someone. And I might add, parenthetically, that in the State of Louisiana I have not been able to find a single person who does not have a friend who knows someone who knows someone who can do something for him. This factor, that is, the pressure of people who have had to do with his election, should not have any influence on the coroner's judgments as to what type of case should be subjected to investigation and what type of investigation should be carried out. The coroner should be free to exert absolutely unbiased scientific opinions on these matters. He should be immune to this type of influence. Let me cite an example of the type of case I have in mind. In a jurisdiction in which I worked, a young man of approximately forty-five years of age was found slumped over his desk in his office one evening when the janitor came to clean. This man happened to be the brother of one of the most important political figures in the state. Investigation showed that the man had been treated by a physician some six months before but when this physician was questioned the treatment had been for an upper respiratory infection and sinusitis and the doctor could not account for the man's death in any way. The medical examiner ordered the body to the morgue for autopsy but before the morguewagon had arrived a funeral director, summoned by the brother, had taken the body to a funeral parlor and had been told by the brother to go ahead with the embalming and that an autopsy was not to be made. The medical examiners, however, had instructed the funeral directors in that state never to embalm a body before they had a bonafide death certificate in their hands and when this action was discovered, and a few harsh words were passed between the medical examiner and this politician, the body was brought to the morgue and an autopsy was performed. The cause of death in this case was cyanide poisoning, suicide, and it is interesting to note that if embalming had taken place the cause of death could not have been discovered, for as you all know, formaldehyde destroys cyanide. I wonder whether the truth in such a case would have been discovered in any jurisdiction from which the members of this audience come or whether this would not have been just another "heart attack."

The fact that the coroner is an elected official means that, once elected, he must not antagonize certain elements in his environment that may be detrimental to his re-election. Very often such influences are not conducive to the best medicolegal practice. Such powerful elements in the community as the press, the funeral directors, the politicians, and the labor unions must be continuously catered to. In the matter of the press, for example, it is frequently not advantageous from the law enforcement point of view to release certain facts to the press prematurely, and yet it is perfectly obvious that in order to gain re-election the coroner must play ball with the press.

Another aspect of the disadvantage of the election of the coroner stems from the fact that a coroner must always seek favorable publicity for re-election. A dramatic case which shows his work in the most favorable

light is a great vote getter. As a result he frequently becomes partisan with the state's attorney and police as a member of the prosecution team rather than maintaining the objective impartially of medical judgement that is of such great importance in medicolegal work. His work appears most favorably in the press and to the public when convictions are obtained. Actually, by impartial and objective fulfillment of his duties in obtaining facts, he should function as much to protect the innocent as to aid in convicting the guilty. By this same token, if prosecution is poor, or police work is poor, his work, although excellent, may appear in a poor light. These factors should have no influence on the re-election of the coroner but the facts are, that under the present system they do. In the best jurisdictions the work of medicolegal investigation goes on quietly and without fanfare or publicity. A case to illustrate this particular point happened in a small county in Maryland. A newly elected district attorney was out to make a reputation for himself and was anxious to get a conviction in the following case. A chronic alcoholic woman was found dead in bed by her similarly afflicted common-law husband after a debauch which had lasted for an indefinite period. The woman showed numerous subcutaneous hemorrhages over exposed parts of her body and rather marked livor mortis. The husband had been arrested, about a year before, for having beaten her when drunk. When questioned this time he stated that he did not beat her but that as he had been drunk it was quite possible that he had. He signed a statement to this effect. The police and the district attorney in the jurisdiction arrested him for homicide. The body was sent for autopsy. At autopsy the woman showed no evidence of injury. The subcutaneous hemorrhages, as you all know, are common findings in people with far advanced alcoholic fatty liver such as she showed. The hemorrhages occur after minor trauma and are due to the liver disease. There was no evidence of strangulation. The immediate cause of death was a severe lobar pneumonia involving both lower lobes. Although appraised of the findings of the autopsy the district attorney, because feelings in the neighborhood ran high and he wished to gain notoriety, decided to prosecute the case anyhow. The defendant had a poor lawyer who did not recognize the importance of the pathological findings. The district attorney decided to prosecute the case without presenting the autopsy findings and to use as evidence the statement of police officers who would testify that the body showed marks of having been beaten when they came upon the scene. The attention of the judge in this case was called by the Chief Medical Examiner of the state to the fact that the autopsy was not going to be introduced in court. The case was dropped and it might be added, the district attorney has resigned his office. In this particular case the accused was a very unpopular character in his neighborhood and I am sure that the fact that the case was dropped because of the action of the Medical Examiner would not have done anything to increase his popularity in that particular district had the facts been known. Not being elected he did not concern himself with local popularity. His action prevented a serious miscarriage of justice.

Another feature of the Louisiana Coroner system which appears to be of doubtful value to the author is the fact that the coroner is charged with duties of commitment of the insane. This feature of the Louisiana Coroner's system is unique in this country. In no other jurisdiction is it expected that someone versed in medicolegal investigation, pathology, and toxicology is also able to qualify as an expert in psychiatry. Such expectations, as we all know, are not realistic. In this day of specialized medicine it need not be emphasized to this group that such a highly specialized field as psychiatry should not be handled by individuals with only minimal training in the field.

The third great disadvantage to the Louisiana Coroner system has to do with budgetary matters. The coroners, particularly in the small parishes, are subject to the whims of the police juries in fiscal mat-

ters. Judgement as to whether a particular case should be investigated by autopsy or toxicological examination is, in great part, influenced by the monetary policies of the particular police jury. Frequently, because of the difficulty in getting examinations paid for, investigations that should be made are not made and those that should be complete are incomplete. Budgetary matters should not influence a medicolegal investigator as to the right course in a particular case. It has been emphasized over and over again by the best authorities in the field that unless cases that are not obvious and cases that are only slightly suspicious are thoroughly investigated in a routine fashion that many murders escape detection or many innocent people are wrongfully accused and even convicted of murder. The costs of medicolegal investigation are not great. In the best jurisdictions the cost of all services in this field comes to approximately five cents per person per year. It is about time that the people of Louisiana were given the best of service along this line in view of the large tax burden that they carry.

ADVANTAGES OF STATEWIDE SYSTEM

What then are the advantages of a statewide system for medicolegal investigation? If properly established, such a system would, in the first place, overcome the three disadvantages outlined in the previous paragraphs. Adequate budget would be provided for the operation of the system and salaries or fees would be made attractive to the most qualified personnel. In establishing such a system the duties of commitment of the insane would be delegated to people well qualified in that field. And most important of all, the system would be removed from the realm of political influence. In Maryland for example a nonpolitical commission of five individuals appoint the Medical Examiners. The positions are career positions, and it should be noted that despite the fact that a complete revolution in politics took place in Maryland in 1950, when Governor Lane, the Democratic incumbent, was defeated by Governor McKeldin, there was no change whatsoever in the personnel, policies or budget of the Maryland Medical Examiner System. Perhaps I am naive, having only recently come to this state, but I still do believe that five people of importance in this state could be found who have no political ties or obligations. I have in mind the Professors of Pathology at the Schools of Medicine within the state or the President of the Bar Association, or the President of the State Medical Association. Such established positions of nonpolitical nature could be made into a commission and the incumbents of such positions might serve during their tenure of office.

There are other advantages in a statewide system for medicolegal investigation as compared to the system in present operation in Louisiana. First and foremost is the fact that the difficulties in obtaining satisfactory investigations in cases that involve one or more parishes at the present time would be overcome. Frequently a patient dies in the Parish of Orleans who had received an injury or become ill in one of the other parishes before being brought to the Parish of Orleans. The difficulty in conducting a proper investigation in a parish where one has no authority is apparent. In a state system such difficulties would be overcome.

Let me give you an outstanding example of how a state system works along these lines. A woman was found on the floor of the front of a large sedan car that rolled down a hill in one of the counties outside of Baltimore. This case was signed out by the police as a death due to vehicular accident and they requested no further examination —it was a clean cut case to them. However, under the system operating in Maryland all violent deaths, including traffic accidents, were subjected to autopsy. When the body was brought to the Baltimore morgue and the blood removed from the face, the wounds on the face had a different appearance. And it was obvious to Dr. Fisher, the Chief Medical Examiner, that this death was not an accident but was murder, "plain and simple, no ifs, ands or buts." Because of the action of the Medical Examiner, pressure was

brought to bear to re-examine the scene and the Medical Examiner in company with police officers went to the scene and then discovered the following interesting facts: Despite the type of injuries on the body, the car was relatively intact. There was no broken glass except for the skylight inside the car. Despite the fact that the body was found on the floor on the front of the passenger's side, the driver's seat had blood which had flowed over the edge of the seat and had flowed in an upward direction if one considers the position in which the car came to rest. If the injuries had been obtained by the impact of the car the blood would have been on the floor and would have flowed to the right rather than to the left. Other evidence were the blood spots on the ceiling of the car; several rows of droplets hitting the roof of the car all in a parallel direction. Perhaps the most damaging bit of evidence was a stone found pressed under the accelerator of the car. When this was discovered it was recalled by the police who came upon the scene that when the car had come to rest, even though Mrs. X was not resting on the accelerator, one of the back wheels that was up in the air was spinning and the police had turned off the ignition switch. The perpetrator of this crime is at present sentenced to be hanged, but I wish to call the attention of this audience to the fact that the murderer probably would not have been apprehended had not the medical examiner been able to cross county lines and to exert his influence on the police in a county of the state. Without this type of examination I am sure this case would have gone down as just another vehicular accident.

Another advantage of having a state system of medicolegal examination is that there will be a certain uniformity of treatment of the citizens throughout the state in the various parishes. For example, if one is driving one's car and a drunk steps off the curb in front of the car and is killed, it is greatly to your advantage at trial to have a determination of the blood alcohol of the deceased victim. As you drive around this state there are some parishes in which this routine examination would be done because there are facilities and funds available and there are other parishes right close by where such an examination would not be carried out. The citizens of this state have the right to expect these facts to be brought forth, and this type uniformity of treatment is almost a necessity.

Perhaps the single greatest asset to be achieved by such a system in this state would be the establishment of a single or group of laboratories around the state qualified to perform toxicological examinations. The usual hospital laboratory is not equipped for this type of examination The tests are highly specialized, the actual amounts of poisons to be discovered in organs or blood are small and they require unusual techniques and specially trained personnel. A laboratory where material for examination from any parish in the state can be sent and the results can be relied upon, will be of great value in improving the practice of forensic medicine about the state. Already there is a section of the coroner's law which makes such a procedure valid and it really only requires activation on a part of the interested parties in the state to get such services going.

A case to illustrate the important information that can be gathered from the performance of routine laboratory determinations follows. A man phoned his neighbor and said that his car was not running that particular morning and would the neighbor be kind enough to pick him up on his way to work. When the neighbor blew his horn outside the man's house the man stepped jauntily from the front door, yelled back an endearing message to his wife and drove off to work with his friend. About an hour after he had left a severe fire broke out in the house and the house was burned to the ground. About eight inches of water accumulated in the cellar and the firemen found the badly burned and charred body of this man's wife in the debris in the cellar. The case would have been dismissed as one of a death due to conflagration except for the fact that in this particular jurisdiction

it was routine to have a carbon monoxide determination done on the blood of the victim of every fire. If a victim is alive during a fire in an enclosed space the blood always contains some carbon monoxide. No carbon monoxide was found in the blood of this woman and on the basis of this, although the exact mechanism of death could not be determined because the body was badly destroyed by fire, a report was made to the police and the fire marshals to make further investigations. The fire marshal discovered a pot-bellied stove in the cellar that had formerly been on the first floor and this stove, peculiarly enough, was melted in several places. The stove was meant to withstand fire and it was quite unusual that a stove of this type should be melted. Further search in the debris revealed an alarm clock mechanism for delayed action. It turned out that the husband had murdered his wife before leaving for work and placed her on the bed as shown in this diagram along with the alarm clock mechanism to set the fire. The bed was loaded with thermite. The heat of the fire destroyed the bed and burned up the evidence of the exact mechanism of death of the woman. The bed, woman, and thermite fell to the first floor onto the stove and subsequently fell into the basement. The friend when questioned stated that he had not seen the wife that morning, nor had he heard her reply to her husband's fond farewell. The husband was convicted of murder. I would like to ask in how many jurisdictions around this state is the determination of carbon monoxide on fire victims a routine procedure? Don't you think the people of this state deserve this kind of medicolegal investigation?

The establishment of a panel of pathologists who would be willing and qualified to do competent examinations under such a system around the state would complete the necessary and important foundation for the establishment of such a system. These pathologists should be adequately recompensed for their service and time in transit. At the Louisiana State University School of Medicine there has been inaugurated a course in Medical Jurisprudence, Toxicology and Traumatic Pathology, which has evoked considerable interest among the students. In addition to didactic teaching, the students are invited to the office of the Coroner of the Parish of Orleans and are given on the scene instruction in the workings of the Coroner's system. Several students have evidenced enough interest to wish to work at the Coroner's office during their summer vacations. Eventually there is hope that a graduate training program in cooperation with the Pathology resident training programs at both medical schools will be inaugurated. This training program should supply a number of qualified personnel throughout the state to carry on under an improved system of medicolegal investigation.

SUMMARY

In summary, I believe that some reform of the existing Coroner's System in Louisiana is indicated. Some specific objectives of such a change have been pointed out. It is not unrealistic to believe that these changes can be made and can be made rather easily. There is a great deal of general interest in medicolegal matters in the state of Louisiana. Much more radical changes have been made in other states where such interest was lacking and where the efforts of the medical profession to improve the situation was combatted tooth and nail by a well established politically strong group of lay coroners. In this state such opposition would not be forthcoming. Already a group of coroners have been questioned on this matter and a majority of them are in favor of it. Any reform of this nature needs the whole hearted support and backing of the medical profession. The exact method of effecting the change in the Coroner system and the details of the change should be worked out by others who have more familiarity with the political workings of the state. In this paper I have merely attempted to point out the advantages to be gained by the inauguration of a state system of medicolegal investigation. Whether such a reform takes place depends in large part upon the interest and efforts of the medical profession.

The Journal of the Louisiana State Medical Society

Established 1844

Published by the Louisiana State Medical Society under the jurisdiction of the following named Journal Committee:

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SUBSCRIPTION TERMS: $4.00 per year in advance, postage paid, for the United States; $4.50 per year for all foreign countries belonging to the Postal Union.

News material for publication should be received not later than the eighteenth of the month preceding publication. Orders for reprints must be sent in duplicate when returning galley proof.

Manuscripts should be addressed to the Editor, 1430 Tulane Ave., New Orleans, La.

THE JOURNAL *does not hold itself responsible for statements made by any contributor.*

THE PHYSICIAN'S INTEREST IN THE PROPOSED BRICKER AMENDMENT TO THE UNITED STATES CONSTITUTION

A condition exists in the treaty-making power of the President of the United States and of the Senate which potentially threatens our rights. Physicians have an interest in this situation as citizens, and they also have an interest in the possible manner in which the treaty-making power may be distorted to utilize the devices of treaty making to precipitate State Medicine upon us.

The concern in this matter arises from the fact that under our law a properly ratified treaty becomes the law of the land and as binding as domestic law. Under such provisions it is conceivable that a president might negotiate a treaty with a foreign power, or with a group of foreign powers, which after ratification would give an outside agency the right to adjudicate matters of dispute between capital and labor, or between races, or in disputes concerning the so-called human rights. The particular occasion for concern is the treaty that already exists between the United States and the International Labor Organization (ILO), of which the United States is a member. To some of its provisions the United States subscribes. The recent resolution by the ILO adopted a convention proposing minimum standards of Social Security, including "socialized medicine." The legal situation is such that our government is under pressure to ratify portions, and possibly, all of this convention.

If that portion proposing socialized medicine should be ratified by the Senate, the national government would then be under solemn obligation to institute all laws and fundamental agencies to carry out this direction, including socialized medicine. If such a circumstance presented, it would establish socialized medicine as a part of our way of life, even after it had been defeated in both Houses of Congress on several occasions in the last ten years, and after the presidential election of 1952, which was practically a referendum defeating this proposal. To meet these very urgent needs and the protection of our rights as citizens, Senator Bricker of Ohio, for himself and sixty other Senators, introduced Joint Resolution No. 1, proposing an amendment to the Constitution of the United States that would limit the present scope of treaties and Executive Agreements. As originally proposed, the amendment would (a) render void any

treaty or executive agreement that denies or abridges any right enumerated in the Constitution; (b) outlaw any treaty authorizing any foreign power or international organization to adjudicate constitutional rights of United States citizens or any domestic issue; and (c) require domestic legislation to permit a treaty to become effective as internal law in the United States.

The administration opposes this amendment on the ground that it would interfere with the treaty-making power of the President, and possibly, interfere with any international agreement which would limit armaments. After other further discussions in the last six months, the wording of the Bricker resolution has been changed, in response to suggestions of an American Bar Association committee. The resolution has been approved by the Senate commtitee, and may be presented to the Senate in the near future. It is probable that long debate will be held, and final action may not be taken before fall.

The opponents of the resolution apparently have brought considerable legal sophistry to bear in combatting it, and their argument may be summed up by saying that the constitutional amendment, if passed, would take power away from those who want to keep the power where it is. Those who are advocating the resolution point to the threat coming from the International Labor Organization's conventions, and to a previous experience, in a case which is described as *Missouri versus Holland*, in which a treaty gave Congress the right to regulate migratory birds for which it specifically did not have any constitutional provision or domestic law.

The American Medical Association has gone on record as being heartily in accord with the purposes of the Bricker Resolution. The Board of Trustees and the House of Delegates of the Association on two occasions have emphatically endorsed the principle that the scope of treaties and executive agreements should be limited. It is the belief of the Association that such a limitation is necessary to avoid any abridgement of the rights enumerated in the Constitution and to prevent adjudication of domestic issues by such measures.

It is quite clear from consideration of the various points raised that our interests as citizens and our desire to avoid State Medicine would both be served by active support of the Bricker resolution.

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ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

LEGISLATIVE ACTIVITY

The Committee on Public Policy and Legislation, under the chairmanship of Dr. Henry W. Jolly, Jr., has asked the cooperation of the component organizations of the State Society to assist in plans for considering various medical matters which will most probably be presented at the next session of the legislature.

It is felt that an intensive public educational program should be undertaken and that this should begin NOW. The president of each component society has been asked to appoint two committees—one to handle contacts with legislators and the other to plan a public educational program. Response to request of the chairman for appointment of these committees has not been very encouraging and in view of the importance of this activity each society is urged to give the matter immediate attention.

Committees appointed at this time are as follows:

CADDO PARISH

COMMITTEE TO CONTACT LEGISLATORS—Dr. S. W. Boyce, Dr. Ford MacPherson, Dr. Clarence Webb.

PUBLIC EDUCATIONAL PROGRAM COMMITTEE—Dr. Keith Mason, Dr. J. P. Sanders, Dr. Jack W. Pou.

CALCASIEU PARISH

COMMITTEE ON LEGISLATIVE MATTERS—Dr. Jared Y. Garber, Dr. Harry S. Snatic, Dr. Melvin H. Gold.

EAST BATON ROUGE PARISH

COMMITTEE ON LEGISLATIVE MATTERS—Dr. Marion Kopfler, Dr. C. S. McConnell, Dr. Agrippa G. Robert, Dr. C. T. Morris, Dr. Albert L. McQuown, Dr. Myron Walker.

ORLEANS PARISH

COMMITTEE TO CONTACT LEGISLATORS—Dr. Edwin L. Zander, Dr. C. J. Brown, Dr. Boni J. DeLaureal, Dr. Charles B. Odom, Dr. H. Ashton Thomas.

PUBLIC EDUCATIONAL PROGRAM COMMITTEE—Dr. Paul L. Getzoff, Dr. William Gillentine, Dr. Nicholas Chetta.

ST. LANDRY PARISH

COMMITTEE TO CONTACT LEGISLATORS—Dr. N. C. Lefleur, Dr. E. K. Ventre, Dr. L. Lazaro, Dr. F. J. Mayer.

PUBLIC EDUCATIONAL PROGRAM COMMITTEE—Dr. W. G. Owen III, Dr. D. J. deBlanc, Dr. W. J. Briley, Dr. F. J. Mayer.

ST. MARY PARISH

COMMITTEE TO CONTACT LEGISLATORS—Dr. Hilton J. Brown.

PUBLIC EDUCATIONAL COMMITTEE—Dr. Giuseppe P. Musso.

WEBSTER PARISH

COMMITTEE TO CONTACT LEGISLATORS—Dr. J. M. Garrett, Dr. B. L. Cook, Dr. Tom Richardson.

PUBLIC EDUCATIONAL PROGRAM COMMITTEE—Dr. C. M. Baker, Dr. Milton Richardson.

MEMBERS OF LOUISIANA STATE MEDICAL SOCIETY WHO DIED

May 1, 1952 to May 31, 1953

Dr. John Bailey Benton, Minden, December 13, 1952.

Dr. E. Oscar Bond, Haynesville, November 21, 1952.

Dr. Joseph Clyde Bruner, Rayne, August 30, 1952.

Dr. Robert McGimsey Carruth, New Roads, November 7, 1952.

Dr. Ronald Eaton Corkern, Natchitoches, February 10, 1953.

Dr. W. E. Dillon, Logansport, September 10, 1952.

Dr. Aurelius Earle Fisher, Monroe, November 7, 1952.

Dr. Simon Geismar, New Orleans, January 4, 1953.

Dr. William Block Heidorn, Shreveport, December 26, 1952.

Dr. James Kirby Howles, New Orleans, April 2, 1953.

Dr. Samuel George Kreeger, Lake Charles, September 1952.

Dr. Leo Douglas Lafargue, Effie, November 24, 1952.

Dr. W. M. Ledbetter, Shreveport, December 2, 1952.

Dr. Willis David Lester, Many, 1952.

Dr. Lionel Francis Lorio, Baton Rouge, June 13, 1952.

Dr. Jesse Woods Mobley, Vivian, 1952.

Dr. Daniel Milton Moore, Monroe, 1953.

Dr. Olin Winn Moss, Lake Charles, January 9, 1953.

Dr. Peter Francis Murphy, New Orleans, November 11, 1953.

Dr. Marvin Milton Odom, Gretna, January 26, 1953.

Dr. Ramon Adrian Oriol, New Orleans, January 5, 1953.

Dr. Alonzo Trent Palmer, Tallulah, October 30, 1952.

Dr. Carl Grisham Pardue, Alto, May 27, 1952.

Dr. Thomas Bryon Pugh, Baton Rouge, May 4, 1952.

Dr. Glenn J. Smith, Amite, May 24, 1953.

Dr. Victor Conway Smith, New Orleans, May 21, 1953.

Dr. John Garrison Snelling, Jr., Monroe, June 22, 1952.

Dr. Benjamin Horace Talbot, Ruston, April 27, 1952.

Dr. James William Tedder, New Orleans, May 5, 1952.

Dr. Clyde Coleman Thompson, Delhi, February 19, 1953.

Dr. William George Troescher, New Orleans, December 31, 1952.

Dr. Martin Thomas Van Studdiford, New Orleans, May 15, 1953.

LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Tuesday of every month	Baton Rouge
Morehouse	Third Thursday of every month	Bastrop
Natchitoches	Second Tuesday of every month	
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

NEWS ITEMS

Dr. T. A. Watters recently attended the monthly meeting of the Chicago Psychoanalytic Society in Chicago and was guest lecturer at the Veterans Administration Hospital in North Little Rock, Arkansas, on May 28-29. While in Little Rock he spoke before the Pulaski County Mental Health Society on "The Mental Health Problem."

Dr. A. Sidney Harris, professor of physiology in the Louisiana State University School of Medicine, will benefit from a grant made recently by Eli Lilly and Company.

The grant will support a study of the action of cardiac drugs under Dr. Harris' direction.

ACTION OF STREPTOMYCIN AND PARA-AMINO SALICYLIC ACID

Streptomycin and PAS are not bacteriocidal but bacteriostatic. They do not cure or eradicate the disease. Relapses occur and reconversion of sputum from negative to positive is frequent. They have markedly improved the prognosis of tuberculosis but have not controlled it. John H. Skavlem, M.D., The W. Va. Med. J., December, 1952.

SYMPTOMS ARE SECONDARY

Many physicians are reluctant to believe that people can have pulmonary tuberculosis when they show no clinical symptoms and there is nothing to direct attention to their lungs except a shadow on a chest film. The tendency is to reassure the patient that the lesions are old and inactive, but the tragedy comes later when the same patient is found to have moderately or far advanced disease. Alan L. Hart, M. D., Public Health Reports, December, 1952.

DEATHS FROM TUBERCULOSIS AND HEART DISEASE

Deaths from tuberculosis among the nation's 88,000,000 life insurance policyholders fell to an all-time low mark in 1952, indicating how effective has been the battle against this long-time scourge, the Institute of Life Insurance reports today.

At the same time, deaths from heart disease among U. S. policyholders reached a record high. Heart disease was the No. 1 killer last year, accounting for well over half of all policyholder deaths.

Tuberculosis, killing nearly one-fourth fewer policyholders than it did the year before, showed the greatest percentage drop of any year on record and accounted for only about 2 per cent of total deaths. The current death rate from this cause is a small fraction of the rate at the turn of the century.

WARN THAT CARBON TETRACHLORIDE POISONING HAZARD IS INCREASING

Carbon tetrachloride, a solvent used extensively as a home and commercial cleaning fluid and for various industrial purposes, is a poison hazard of increasing importance, according to a warning sounded in an article in the American Medical Association's Archives of Industrial Hygiene and Occupational Medicine.

The deadly effects from inhaling the fumes or swallowing the product were related by two United States Public Health surgeons, Dr. Albert V. Myatt of the malaria project at the federal penetentiary in Atlanta, and Dr. James A. Salmons of the U.S. Public Health Service Hospital in San Francisco. One finding of a joint study was that persons drinking alcoholic beverages are more likely to be affected.

They reported that 15 persons suffering from carbon tetrachloride poisoning were admitted to the San Francisco Hospital from January, 1948, to May, 1951, an incidence of about one per 1,000 admissions. Of these, three died and the others recovered. Seven patients were seamen electricians who used the product to clean motors; three other patients used it as a degreaser. Three swallowed the solvent; case histories were not obtainable in two others.

"The public believes carbon tetrachloride to be a relatively safe cleaning agent," the surgeons reported. "Its noninflammability is one reason for its widespread use. The average nonmedical user does not know that the toxicity of carbon tetrachloride is enhanced in alcoholics or in malnourished persons.

DOCTORS NEEDED

Louisiana Ordnance Plant, Remington Rand, Inc. Shreveport, Louisiana. Family man, under sixty years of age, preferred. Salary $8,500.00.

New clinic in Oberlin, Louisiana available rent-free. If desired equipment will be furnished at small rental fee. Contact American Legion Post No. 144, Oberlin in care of Allen J. Fuselier.

UROLOGY AWARD

The American Urological Association offers an annual award of $1000.00 (first prize of $500.00, second prize $300.00 and third prize $200.00) for essays on the result of some clinical or laboratory research in Urology. Competition shall be limited to urologists who have been in such specific practice for not more than ten years, and to men in training to become urologists.

The first prize essay will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Waldorf-Astoria, New York City, May 31-June 3, 1954.

For full particulars write the Executive Secretary, William P. Didusch, 1120 North Charles Street, Baltimore, Maryland. Essays must be in his hands before February 1, 1954.

STEWART GORDON THOMPSON, D.P.H.

1881-1953

Announcement has been received from the Florida Medical Association that Dr. Stewart Gordon Thompson, Managing Director of that Association for over a quarter of a century, died on April 23, 1953.

BOOK REVIEWS

Endocrine Functions of the Pancreas; by Bernard Zimmermann, M. D. Springfield, Ill., Charles C. Thomas, 1952. Pp. 82. Price $2.50.

This is a monograph in the American Lecture Series and represents a particularly well organized presentation of the available material. The monograph begins with a brief history of experimental pancreatic diabetes, the discovery of insulin and of other endocrine glands involved in the regulation of carbohydrate metabolism. This is followed by a short but adequate review of the nature of insulin. The metabolism in diabetes and the various theories concerning the etiology of diabetes are reviewed as is the action of insulin in alleviating diabetes. The last three chapters are concerned with the regulation of internal pancreatic secretion, special problems in lipid metabolism and the hyperglycemic factor. The latter chapter is particularly well written and the author points out that there is still insufficient evidence to indicate whether this factor is truly an alpha-cell hormone or an endocrine substance at all. On the other hand, the presence of a blood sugar-elevating principle in insulin preparations does reconcile some of the conflicting evidence regarding the action of insulin. While the primary emphasis is on experimental data, the author does include many clinical considerations and applications which will make the monograph of interest to clinicians as well as to investigators. While much of the material is available in the usual texts, this monograph serves as an excellent brief but critical review. There is also an extensive bibliography at the end of each chapter.

H. S. Mayerson, Ph. D.

Atlas of Medical Mycology; by E. S. Moss, M. D., and A. L. McQuown, M. D. Baltimore, Williams & Wilkins, 1953. Pp. 245. Price $8.00

Here is a book written by clinicians for the use of clinicians. It is an excellent and thorough pictorial presentation of every aspect of the field of medical mycology, with particular emphasis on clinical and mycological methods of diagnosis. The text is perhaps somewhat sketchy but one must bear in mind that the primary intent of the authors was to simplify as much as possible the numerous problems encountered in the diagnosis of fungous disease by the clinician who lacks specialized training in this field. They have succeeded admirably in accomplishing this purpose.

The book contains some 248 outstanding photographs and photomicrographs. These have been carefully selected so that, for each type of fungous disease, there is illustrated: (a) the gross appearance of the lesions, (b) the appearance of the etiologic agent in transudates and exudates, (c) the histopathology, and (d) the gross and microscopic characteristics that serve as a basis for identification of the etiologic agent after isolation in culture. There is also a section illustrating the characterstic features of many species of fungus contaminants. All diseases known to be caused by fungi are adequately presented.

It is felt that this book fills a definite need and deserves a place in the library of not only the clinical pathologist and dermatologist but of the general practioner as well.

J. D. Schneidau, Jr.

Intracranial Aneurysms: By Wallace B. Hamby, M. D. Springfield, Illinois, Charles C Thomas, 1952. Pp. 564, illus. Price $14.25.

Increasing surgical interest in cerebral vascular lesions is reflected in this handsome volume which includes in its purview intracranial arterial aneu-

rysms, arteriovenous fistulae and angiomatous malformations. By far the largest part of the book concerns the first of these three, and only a small section is devoted to the last.

Improved diagnosis of intracranial vascular lesions since the advent of cerebral angiography has placed the onus of treatment more squarely on the shoulders of the clinician. Dr. Hamby has surveyed the literature of the field from the neurosurgeon's point of view, bringing his critical judgment to bear on the available evidence. He has done an important service by summarizing the background necessary for understanding current treatment. The views of such outstanding contributors as Dandy, Jefferson, Olivecrona and Poppen are given prominence while Dr. Hamby's own cases provide additional samples of the problems to be faced. Recent references that have not been integrated into the text are included in the bibliography. The section on prognosis of subarachnoid hemorrhage is important for clinical observers who see this entity, if no other section of the book is read.

The continued use of the test for collateral cerebral circulation published by Dr. Rudolph Matas, in 1910, will be of particular interest to those who have worked with him. Tantalum bands for partial or transient carotid ligation have been substituted for the aluminum ones of Dr. Matas described in 1911. Selverstone's new clamp which can be occluded progressively or opened quickly without re-exposing the artery, while not described in the text, is the most recent step. It is a modification of Goldblatt's renal artery clamp used in the experimental production of hypertension.

Since publication, cerebral circulatory physiology, which is treated briefly, has had several important additions. Of particular interest are intracranial arterial pressure measurements recorded by Woodhall during surgical exposure of aneurysms and cerebral blood flow measurements by Shenkin after carotid ligation for aneurysm. An understanding of the contraindications to cerebral angiography also has progressed and the effect of intra-arterial diodrast on cerebral tissue has been studied intensively. Complications of carotid artery ligation in the neck for intracranial vascular lesions have been analyzed further by Brackett and additional experiences with intracranial trapping procedures utilizing controlled blood pressure have been presented, particularly by Poppen.

W. RANDOLPH PAGE, M. D.

Penicillin Decade, 1941-1951; Sensitizations and Toxicities; by Lawrence W. Smith and Ann D. Walker. Washington, D. C., Arundel Press Inc., 1952. Pp. 122. Price $2.50.

A thorough and useful compilation of all types of toxic reactions reported as occurring in patients after administration of penicillin preparations. The reactions following the early crude preparations, the suspensions of penicillin in peanut oil and beeswax and pure crystalline procaine-penicillin G are described.

Discussions of sensitization to pure penicillin preparations by topical application in therapeutically inadequate amount, consideration of special factors involved in administration of penicillin to infants and children, development of bacterial resistance and similar things add to the value of the book.

FOSTER N. MARTIN, JR., M. D.

The Clinical Use of Testosterone; by Henry H. Turner, M.D. Springfield, Illinois, Charles C Thomas, Publisher, 1950. pp. 69. Price $2.00.

This volume consolidates and brings to the point of usefulness many isolated facts which most of us know but do not apply. Before and after pictures of patients with various types of hypogonadism help out the text considerably. One of its attributes is that it does not limit itself to positive indications for the use of testosterone, but speaks out against its use in benign prostatic hypertrophy, impotence due to psychic causes, and certain other borderline conditions.

The repeated warnings of the author concerning the "unfortunate misinformation regarding male hormonal therapy which has been fostered, exaggerated, and frequently misstated by sensational and pseudoscientific lay writers" is applauded.

The book is not limited to therapeutics; it discusses in some detail the history, physiology, chemistry, and metabolism of testosterone. Of use to the clinician is a chapter at the end of the book on commercial preparations of testosterone.

This valuable book is further enhanced by its complete bibliography.

J. W. VILDIBILL, JR., M.D.

Tobacco and the Cardiovascular System; by Grace M. Roth, Ph.D. Springfield, Illinois, Charles C Thomas, Publisher, 1951. pp. 66. Price $2.25.

This presentation is short and concise. The history of the problem is reviewed briefly and data are presented to illustrate the effects of smoking on heart rate, blood pressure, skin temperature, and the electrocardiogram control tests included the use of "denicotinized" tobacco, various types of paper, mechanical act of smoking and intravenous injection of nicotine. These various procedures lead to the conclusion that nicotine is the "offending" agent with a resultant vasoconstriction. That this occurs seems quite clear from the data presented but that it is detrimental is not quite so clear.

There are an adequate number of charts and diagrams to illustrate the points which the author makes. The presentation is quite clear and well organized. This monograph is to be recommended for anyone interested in vascular responses.

CLARENCE THORPE RAY, M.D.